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Acetyl chloride as a polar solvent. Part II. Solvolytic reactions in acetyl chloride. By RAM CHAND PAUL, DULA SINGH, and SARJIT SINGH SANDHU

Co-ordination of trimethylamine by halides of silicon, germanium, and tin. By J. E. FERGUSSON, D. K. GRANT, R. H. HICKFORD, and C. J. WILKINS

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The Perkin reaction. Part I. Aliphatic aldehydes. By MALCOLM CRAWFORD and W. T. LITTLE

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Triazaphenanthrenes. Part III. Synthesis of some 9-aryl-2 : 3 : 10-triazaphenanthrenes. By C. M. ATKINSON and R. E. RODWAY

Triazaphenanthrenes. Part IV. Some 9-aryl-3-methyl-1 : 2 : 10-triazaphenanthrenes. By C. M. ATKINSON and R. E. RODWAY

Studies of the chemical effects of γ-radiation on organic systems. Part I. Studies of the systems pyridine–bromobenzene and aniline–bromobenzene. By G. A. SWAN and P. S. TIMMONS

Studies of the chemical effects of γ-radiation on organic systems. Part II. The action of radiation on benzyl alcohol alone or mixed with acetone or bromobenzene. By G. A. SWAN and D. WRIGHT

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Some chloride alkoxides of quadrivalent vanadium and quinquevalent molybdenum. By D. C. BRADLEY, R. K. MULTANI, and W. WARDLAW

Chloroalkoxides of titanium, zirconium, cerium, and thorium. By D. C. BRADLEY, R. N. P. SINHA, and W. WARDLAW

Stereochemical investigations of cyclic bases. Part IV. Hofmann degradation of 6α- and 6β-cholestanyltrimethylammonium salts. By B. B. GENT and J. MCKENNA

Cyto-active amino-acids and peptides. Part V. Derivatives of *p*-amino- and *p*-mercapto-phenylalanine. By F. BERGEL and J. A. STOCK

Cyto-active amino-acids and peptides. Part VI. Synthesis of *N'*-α-aminoacyl-*NN*-di-(2-chloroethyl)-*p*-phenylenediamines. By F. BERGEL and J. A. STOCK

cis-trans-β-Methylmuconic acid. By J. A. ELVIDGE

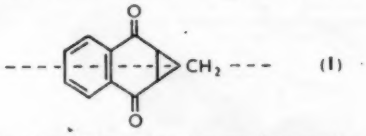
The hydrolysis of ethyl 3-oxo-octadecanoate. By D. W. S. EVANS

767. *The Crystal Structure of* 2 : 3-*Dihydro*-2 : 3-*methylene*-1 : 4-*naphthaquinone.*

By W. K. Grant and J. Clare Speakman.

The compound (I) crystallises in a form that is convenient for structure analysis by *X*-ray diffraction. The crystals belong to the monoclinic system, with $a = 6{\cdot}98$, $b = 10{\cdot}55$, $c = 5{\cdot}46$ Å, and $\beta = 94\frac{1}{2}°$, and there are two molecules in the unit cell, with the space group $P2_1/m$. The molecule is bisected by a crystallographic plane of symmetry. The benzenoid ring, which lies perpendicular to this plane, is itself coplanar; but the quasi-quinonoid residue is non-coplanar, and the two carbonyl bonds are not collinear. Bond lengths and bond angles have been determined with moderate accuracy, including those in the three-membered ring; and the stereochemistry has been studied in some detail at the heavily strained carbon atoms by which this ring is fused to the naphthaquinone system.

2 : 3-Dihydro-2 : 3-methylene-1 : 4-naphthaquinone (I), prepared and described by Buchanan and Sutherland,[1] is of uncommon interest for metrical study because it includes a three-membered ring—very few examples of which have been studied—and because the



(I)

carbon atoms by which this ring is fused to the naphthaquinone residue must be under severe strain. Fortunately its crystal structure is favourable for study by *X*-ray methods. In three independent projections the atoms are usefully resolved, so that two-dimensional methods of analysis are likely to be unusually effective. A progress report on this work has been published.[2]

Experimental

Crystallographic Data.—The material used was kindly supplied by Dr. G. L. Buchanan; it had been recrystallised from toluene and melted at 128—130°. The crystals showed straight extinction in polarised light, and formed laths with pointed or wedge-shaped ends, elongated in the direction of *b*. The (100) pinakoids were most prominent, and the domes (011) and/or (110) were usually present; (001) pinakoids were sometimes recognisable. The following unit-cell parameters were derived from single-crystal rotation, oscillation, and moving-film photographs, copper-K_α radiation being used throughout: $C_{11}H_8O_2$, Mol. wt. = 172·2. *Monoclinic prismatic*, $a = 6{\cdot}98$, $b = 10{\cdot}55$, $c = 5{\cdot}46$ Å (each $\pm 0{\cdot}02$ Å), $\beta = 94\frac{1}{2}°$, volume of unit cell = 400·9 Å^3, density measured by flotation = 1·40 g./c.c., density calculated for *two molecules* per cell = 1·426, absorption coefficient for *X*-rays = 9·2 cm.$^{-1}$, $F(000) = 180$. *Absent reflexions* are $0k0$ when k is odd, implying that the space group is either $P2_1$ (C_2^2) or $P2_1/m$ (C_{2h}^2). The Wilson ratio, $N(z)$, and variance tests were applied to the intensity data in the $hk0$-zone, and they all unambiguously indicated centro-symmetry. Furthermore, when placed on the same scale, average intensities in the $h0l$ zone were greater than those in $hk0$ by a factor of about two; this is evidence for a plane of symmetry perpendicular to *b*, which again implies centro-symmetry. The *space group* $P2_1/m$ was therefore adopted, and the subsequent progress of the analysis corroborated the choice.

This space group requires the presence of mirror-planes at $y = \frac{1}{4}b$ and $\frac{3}{4}b$; and two molecules of formula (I) can be accommodated only if they are each bisected by one of these planes in the manner suggested by the broken line. It follows that the crystal structure is a simple one, for which preliminary *y*-co-ordinates could at once be written down from a knowledge of standard bond-lengths.

[1] Buchanan and Sutherland, *J.*, 1954, 1060; 1956, 2620.
[2] Grant, Vos, and Speakman, *Acta Cryst.*, 1957, **10**, 806.

XUM

Structure Analysis.—The multiple-film technique was used to measure the intensities of some 189 independent reflexions in the three principal zones, out of about 234 accessible to copper radiation. The crystals used had dimensions of the order 0·2 mm., so that absorption

FIG. 1. *Electron-density projections along the c-, a-, and b-axes. (The contour-lines are at intervals of 1 electron per sq. Å, with the zero-line broken.)*

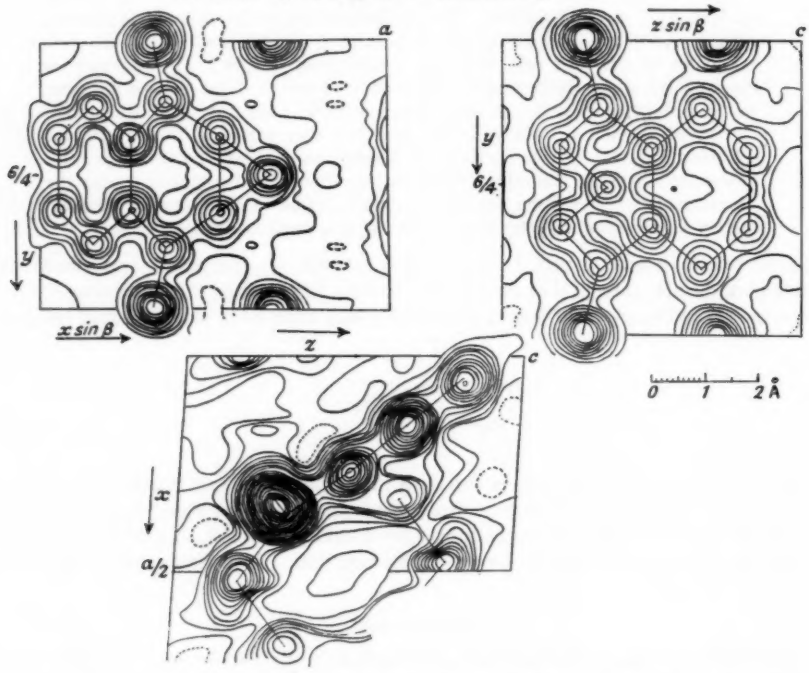


TABLE 1. *Atomic co-ordinates (x, y, and z, as fractions of unit-cell edges), values of the "reliability index" (R), and Debye temperature factors (B, in Å²) for the three independent zones.*

Zone	*hk*0		*h*0*l*		0*kl*	
	x	*y*	*x*	*z*	*y*	*z*
O	0·327	0·003	0·330	0·270	0·000	0·270
C(1)	0·050	0·182	0·047	0·830	0·182	0·833
C(2)	0·150	0·120	0·150	0·667	0·117$_5$	0·670
C(3)	0·263	0·182	0·267	0·503	0·183	0·507
C(4)	0·363	0·115	0·363	0·327	0·115	0·327
C(5)	0·523	0·177	0·523	0·190	0·175	0·190
C(6)	0·667	0·250	0·667	0·347	0·250	0·347
R	0·130		0·113		0·122	
B_O	Ranging from 3·5 parallel to *x* to 2·5 parallel to *y*		3·5		Ranging from 3·5 parallel to *z* to 2·5 parallel to *y*	
B_C	2·8		3·3		2·8	

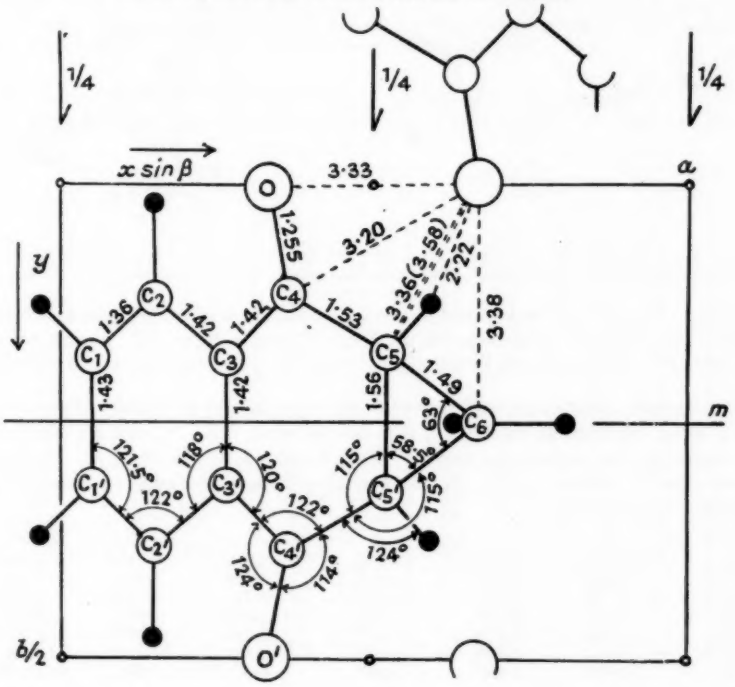
of *X*-rays would be small and was neglected. Trial structures were found for each axial projection and refined in the usual way by double Fourier series. The final electron-density calculations were made on the digital computer designed by Robertson,[3] and completed in a total time of about 8 hr. The results are displayed in the maps reproduced in Fig. 1. All the

[3] Robertson, *Acta Cryst.*, 1954, **7**, 817; 1955, **8**, 286.

atoms, other than hydrogens, are resolved in the projections along a and c; whilst along b all pairs of atoms related by the mirror-plane are precisely superposed and are represented by discrete peaks of double height, apart from the partial overlap of the four atoms of the carbonyl groups. To have effected substantial resolution of the atoms in all three projections is remarkable with a non-coplanar molecule of this type, and it opened the possibility of attaining moderate accuracy of analysis without recourse to three-dimensional methods.

Further refinement was by repeated " difference " syntheses. Standard atomic-scattering functions [4] were used; they were modified by Debye temperature factors, with the B-values shown in Table 1—isotropic for carbon, and usually anisotropic for oxygen. The direction of the anisotropy is consistent with some libration of the molecule about its centre of mass.

FIG. 2. *The molecule and some of its environment in the c-axis projection, showing the numbering of the atoms, interatomic distances* (Å), *and bond-angles.*



Each principal projection of the structure was refined independently. For this reason observed, F_o, and calculated, F_c, values of the structure amplitudes for reflexions common to two zones are not quite identical in each, though only with $F(100)$ is the difference other than trivial.

At an early stage of the refinement hydrogen atoms were introduced in plausible positions and their introduction sensibly improved the agreement between F_o and F_c. In difference syntheses, where only the contributions due to carbon and oxygen atoms had been subtracted, peaks with heights of 0·6—1·0 electron per sq. Å appeared at the expected positions; but they were not definitive enough to warrant their use in any systematic emendation of the hydrogen co-ordinates.

Results.—Final atomic co-ordinates for each projection are listed in Table 1, which also shows values of R, the " agreement index." The numbering of atoms is explained in Fig. 2; the hydrogen atoms are numbered according to the adjacent carbon atom. Mean values of these (fractional) co-ordinates are given in Table 2, in which also appear co-ordinates (X', Y, and Z', in Å) with respect to orthogonal axes. Final values of observed structure amplitudes

[4] Berghuis, Haanappel, Potters, Loopstra, MacGillavry, and Veenendaal, *Acta Cryst.*, 1955, **8**, 478.

and calculated structure factors are collected in Table 4. Unobserved reflexions are omitted; only in 10 cases out of 45 did the magnitude of F_c imply that the reflexion should have been just detectable. The bond-lengths and angles derived from the co-ordinates in Table 2 are shown in Fig. 2. All intermolecular contacts, except those shown specifically, exceed 3·4 Å. The general conformation of the molecule is demonstrated by the perspective sketch in Fig. 3*a*; the viewer is supposed to be looking down at an angle of about 45° on to the equatorial plane of molecular symmetry.

Accuracy.—Two methods for assessing accuracy are applicable here. First, since every

FIG. 3*a*.

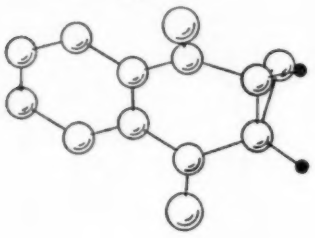


FIG. 3*b*.

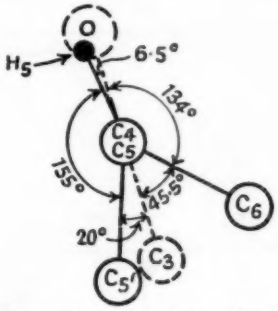


FIG. 3. (*a*) *A perspective view of the molecule.* (*b*) *Distribution of bonds about* C(4) *and* C(5), *as viewed along the direction of the bond between these two atoms; the dihedral angles are shown.*

atomic co-ordinate has been determined in two independent zones, corresponding values can be compared. The standard deviations (σ) of the co-ordinates from their means are given in Table 3, row (*a*). The estimates thus derived for the six carbon atoms, taken together, were

TABLE 2. *Atomic co-ordinates, with respect to an origin located at a centre of symmetry, x, y, and z being expressed as fractions of the unit-cell edges. X', Y, and Z', which are in* Å, *are measured along orthogonal axes, X' being parallel to x, and Y to y. The numbering of the atoms is shown in Fig.* 2; *the hydrogen atoms are numbered according to their respective carbon atoms.*

Atom	*x*	*y*	*z*	*X'*	*Y*	*Z'*
O	0·328$_5$	0·001$_5$	0·270	2·177	0·016	1·470
C(1)	0·048$_5$	0·182	0·831$_5$	−0·018	1·920	4·526
C(2)	0·150	0·118$_5$	0·668$_5$	0·761	1·253	3·639
C(3)	0·265	0·182$_5$	0·505	1·633	1·925	2·749
C(4)	0·363	0·115	0·327	2·394	1·213	1·780
C(5)	0·523	0·176	0·190	3·569	1·857	1·034
C(6)	0·667	0·250	0·347	4·507	2·638	1·889
H(1)	−0·03	0·13	0·97	−0·64	1·40	5·26
H(2)	0·15	0·02	0·67	0·76	0·18	3·64
H(5)	0·59	0·12$_5$	0·03	4·13	1·32	0·18
H(6)	0·63	0·25	0·53	4·26	2·64	2·89
H(6')	0·81	0·25	0·33	5·40	2·64	1·80

TABLE 3. *Estimates of the standard deviations* (σ) *in the final atomic co-ordinates* (Å); *σ(r) is the R.M.S. positional deviation.*

		σ(x)	*σ(y)*	*σ(z)*	*σ(r)*
(*a*)	C and O atoms	0·0080	0·0101	0·0063	—
(*b*)	C atoms *hk*0	0·020	0·022	—	—
	C atoms *h*0*l*	0·008	—	0·008	—
	C atoms 0*kl*	—	0·009	0·012	—
	O atom *hk*0	0·009	0·010	—	—
	O atom 0*kl*	—	0·004	0·005	—
(*c*)	R.M.S. values C	0·0133	0·0149	0·0090	0·0126
	R.M.S. values O	0·0085	0·0085	0·0057	0·0082

hardly affected if the deviation for the oxygen atom was also included; and, since the data for this atom were not sufficiently numerous to warrant separate consideration, the standard deviation based on all seven atoms has been adopted for both carbon and oxygen. Secondly, as the resolution is so good, Cruickshank's method [5] can be applied with confidence, and it leads to the σ-values shown in the Table, row (*b*). The σ-values thus derived are decidedly least favourable for the zone giving the best projection of the molecule, though the *R*-value is hardly inferior. This typical result can be related to the larger number of reflexions in the *hk*0-zone. Root-mean-square deviations, based on the three independent estimates, appear in the last row (*c*) of Table 3.

These last standard deviations of co-ordinates have been used to assess σ-values for bond-lengths and angles: σ(C–O) = ±0·015 Å; σ(C–C) = ±0·018 Å in general, but for the bonds, such as C(1)–C(1′), lying across the plane of symmetry, C–C depends only on the *y*-co-ordinate, and σ(C–C) is then ±0·030 Å. For a bond-angle (θ) near to 120°, σ(θ) = ±1·1°. The positions of the hydrogen atoms are known only roughly, for the reasons already given. It is possible that they have been located within 0·2 Å of their correct positions.

TABLE 4. *Observed structure amplitudes and calculated structure factors. (In each set of three columns, the first lists the value of the varying index, the second* $|F_o|$*, and the third* F_c*.)*

*hk*0-zone

	0*k*0																	
			8	4·2	−3·8	9	1·6	−0·3	12	2·9	+2·9	2	1·9	+0·9	8	6·6	+6·8
2	12·5	−14·1	9	3·3	+2·3	10	3·3	−2·4				3	14·2	+13·5	9	1·4	+2·3
4	3·8	−2·1	10	2·8	−1·0	11	2·1	+1·5		4*k*0		4	7·0	−6·9			
6	25·0	+24·6	11	6·8	−6·0				0	3·1	−4·4	5	3·4	−3·2		7*k*0	
8	8·1	+6·9	12	3·5	−2·8		3*k*0		1	8·2	−7·9						
10	11·5	+10·4	13	1·1	+0·2	0	23·2	+22·6	2	14·3	−12·9	6	8·2	−7·0	0	3·5	−3·0
12	4·0	+3·4				1	1·3	+0·6	3	2·8	+2·0	7	8·2	−7·8	1	3·5	+3·6
				2*k*0		2	10·5	+10·5	4	2·9	−1·6	8	2·7	+1·7	2	1·2	+2·2
	1*k*0		0	12·2	−11·9	3	5·8	−6·2	5	4·8	+5·6	9	3·0	+2·8	3	2·2	−1·7
0	17·1	−17·1	1	21·7	−19·8	4	18·7	+17·4	6	9·7	+8·7	11	2·3	+3·5	7	0·7	−1·3
1	28·4	−29·6	2	18·1	−16·5	5	1·0	+1·6	7	9·9	−10·5						
2	6·4	−5·9	3	9·2	+6·7	6	2·7	+2·7	8	14·3	−13·4		6*k*0			8*k*0	
3	23·9	−23·0	4	12·3	−12·0	7	7·2	+7·0	9	4·6	+4·6	0	8·0	+9·5	0	0·9	+1·8
4	8·2	−8·2	5	0·9	+0·8	8	7·6	+7·5	12	1·9	+4·7	1	4·5	−3·8	1	4·6	−6·6
5	15·0	+15·0	6	1·5	−1·0	9	2·2	−0·8				2	4·6	+4·7	2	0·7	−0·9
6	4·6	−3·3	7	2·3	−1·4	10	5·7	+2·2		5*k*0		4	0·9	+1·6	3	1·0	+1·4
7	2·7	−4·1	8	9·1	−10·8	11	1·4	+2·0	0	8·5	−11·3	5	1·9	+2·5	4	2·5	−4·0
									1	3·0	−1·9	6	1·1	−0·2	5	0·9	+2·8

*h*0*l*-zone

	00*l*																	
			0	24·2	−22·5	1	66·0	+76·3	2	8·2	+6·4	3	18·1	−12·8	0	10·7	+11·0
1	32·3	−32·1	1	3·4	+4·9	2	20·3	−25·7	3	3·5	+3·2				1	3·1	−4·2
2	35·2	−36·6	2	11·8	+11·6	3	19·9	−19·9	4	2·5	−1·0		50*l*		2	6·2	−6·2
3	4·6	+4·3	3	8·0	+7·7	5	6·7	+8·1	5	6·2	−6·8	3	9·2	+8·9	3	12·4	+11·1
4	5·5	+4·4	4	10·9	−10·5	6	2·3	−2·3				2	3·8	−3·7	4	7·8	−4·8
5	6·3	−6·4	5	5·3	−5·2					40*l*		1	10·5	−9·6			
6	10·4	+10·4	6	2·9	+3·2		30*l*		5	5·5	+5·7	0	9·9	−10·7		70*l*	
						5	3·3	−2·5	4	10·2	+9·3	1	15·5	+14·5	2	3·3	+2·7
	10*l*			20*l*		4	9·2	+8·3	3	21·2	−25·3	2	11·4	+10·4	1	3·2	−5·0
8	1·9	−1·7	8	2·7	+2·9	3	6·2	+6·0	2	2·9	+4·0	4	5·5	−5·7	0	3·2	−3·1
5	6·3	+6·2	5	11·6	+11·2	2	16·5	−14·8	1	16·1	+15·1						
4	3·1	−1·4	4	18·8	−14·6	1	14·7	−14·8	0	2·8	−4·4		60*l*			80*l*	
3	15·6	−14·6	3	8·1	+6·5	0	26·1	+24·7	1	6·6	−6·5	3	6·0	+5·9	3	2·2	+3·4
2	11·8	+11·1	1	6·9	−8·4	1	2·1	−1·1	2	19·1	+19·0	2	12·8	−14·6	1	2·5	−4·6
1	10·2	+14·5	0	14·5	−13·2												

0*kl*-zone

	0*k*0		3	5·5	+5·4	3	8·0	−8·4	2	16·9	+17·7	5	1·3	−2·0		0*k*6	
2	15·8	−17·3	4	1·0	−1·4	4	6·3	−7·3	3	1·7	+0·6	6	9·3	+6·9	0	9·0	+8·7
4	3·5	−5·0	5	3·3	−2·9	5	4·5	+5·8	4	4·1	−2·2	7	2·6	+1·3	2	3·2	−4·1
6	25·8	+25·4	6	1·8	+3·0	6	8·6	−8·3	5	1·9	−3·1	8	1·5	−0·9	3	1·1	+1·1
8	9·5	+8·2	7	1·6	+1·6	7	2·6	−2·0	6	14·1	−14·1	10	1·2	+1·1	4	3·1	−4·1
10	11·6	+9·3	8	4·7	−5·0	8	12·5	−10·5	7	1·9	+2·8						
12	3·3	+3·1	10	2·3	−2·9	10	4·4	−3·8	8	18·1	+17·0		0*k*5				
						12	1·2	−1·1				0	5·2	−5·3			
	0*k*1			0*k*2						0*k*4		2	3·2	−3·2			
0	32·6	−30·5	0	33·7	−36·1		0*k*3		0	4·0	+3·8	5	1·4	+1·3			
1	8·9	−7·8	1	7·4	+7·7	0	3·6	+3·6	2	3·4	+5·8	7	1·2	−1·5			
2	1·9	+2·7	2	17·6	−17·5	1	3·8	+4·2	4	3·5	+6·1	8	2·6	−2·6			

DISCUSSION

The structure found for this molecule will be discussed in three aspects: the naphthaquinone residue; the *cyclo*propane ring; and the valency distribution about the heavily strained atom, C(5).

[5] Cruickshank, *Acta Cryst.*, 1949, **2**, 65.

Benzoquinone is one of the fundamental aromatic structures analysed by Robertson.[6] His *X*-ray measurements have recently been recalculated by Trotter,[7] using current methods of refinement. The molecule is centrosymmetric, so that the two C–O bonds are necessarily parallel; and in fact they are collinear within close limits, the molecule being virtually planar. The bond lengths, now amended, are C=O = 1·19, C–C = 1·49, and C=C = 1·31 Å, each with an estimated standard deviation of ±0·03 Å. An electron-diffraction study of the molecule in the gaseous state [8] yielded results in good agreement, *viz.*, C=O = 1·23, C–C = 1·49, C=C = 1·32 Å. Anthraquinone has a similar structure according to Sen's determination,[9] which corrected an earlier study: the molecule is centrosymmetric and virtually coplanar, with C–C = 1·39 in the benzenoid rings, C=O = 1·15, and C–C adjacent to the carbonyl groups = 1·50 Å. Bailey's careful analysis of the large molecule indanthrone [10] led to similar results in the anthraquinone residues, with C–O = 1·20—1·23 Å; the same author finds C–O = 1·25 Å in her recent work on 1 : 5-dichloroanthraquinone.[11]

The most obvious difference between these structures and that now found for molecule (I) is the non-collinearity of the C–O bonds. The deviation is evident in both *a*- and *c*-axis projections (Fig. 1), and at the oxygen atom it amounts to nearly 0·4 Å, which is highly significant. [The dihedral angle between C(2)–C(3) and C(4)–O about C(3)–C(4) is 14°.] There is distortion of the carbonyl bonds in 1 : 5-dichloroanthraquinone too; this is due to steric repulsion between oxygen and chlorine atoms. The distortion of the quasi-quinonoid part of molecule (I) is qualitatively similar to that observed in each anthraquinonoid moiety of dianthronylidene (dianthrone).[12] But, as dianthrone is a typically over-crowded molecule and (I) is not, the causes of the distortion must differ. Two intramolecular factors may operate to maintain molecule (I) in its configuration: (*a*) the difference (~0·2 Å) between the lengths of bonds C(3)–C(3′) and C(5)–C(5′) will tilt the carbonyl groups towards the benzenoid ring; (*b*) the *cis*-fusion of the three-membered ring forces carbon atoms 5 and 5′ to adopt an eclipsed conformation, and the angle C(4)–C(5)–C(5′) is much less than 120°, for which reasons the atoms 4, 5, 5′ and 4′ take up positions resembling those of carbon atoms in (half of) a *cyclo*hexane molecule in its less stable, " boat " form; and hence the C–O bonds are tilted towards positions that would be those occupied by the " bowsprit " of the boat. The conformation may also be sustained by an intermolecular factor. The hydrogen atom attached to C(5) is directed very nearly towards the oxygen atom of a neighbouring molecule, as is shown in Fig. 2; the total separation C(5) · · · O″ is 3·36 Å, whilst H · · · O″ is about 2·2 Å. This might represent hydrogen bonding, which—though very weak—would be sufficient to exert an influence on the C–O-bond, and to fix its orientation about the C(4)–C(5)-bond. That compound (I) melts at a temperature 50° higher than its homologue, in which these two hydrogen atoms are replaced by methyl groups,[1] may possibly be related to this intermolecular bonding. (O″ belongs to the neighbouring molecule at the top of Fig. 2.)

The bond C(3)–C(4) is significantly shorter than is the corresponding bond in benzoquinone, and the carbonyl bond is possibly significantly longer. These differences would imply that there is more conjugation here between the aromatic ring and the carbonyl group than is normal in a quinone. This is also in accord with the angles round C(4). At first sight a lengthening in the ketonic group might be expected to be accompanied by a diminution of the C–O stretching frequency. But the band at 1675 cm.$^{-1}$ assigned to this vibration is at a slightly higher frequency than the cognate band in the spectrum of benzoquinone (1667 cm.$^{-1}$). However the carbonyl stretching frequency is insensitive to small

[6] Robertson, *Proc. Roy. Soc.*, 1935, *A*, **150**, 106.
[7] Trotter, Thesis, Glasgow, 1957.
[8] Swingle, *J. Amer. Chem. Soc.*, 1954, **76**, 1409.
[9] Sen, *Indian J. Phys.*, 1948, **22**, 347.
[10] Bailey, *Acta Cryst.*, 1955, **8**, 182.
[11] *Idem*, *ibid.*, 1958, **11**, 103.
[12] Harnik and Schmidt, *J.*, 1954, 3295.

changes in length.[13] (In a personal communication Dr. Bailey informs us that this frequency lies at 1680 cm.$^{-1}$ in solid 1 : 5-dichloroanthraquinone, a value which hardly differs from that in anthraquinone, 1678, though the bond in the chloro-compound is longer). It is possible that the environment has a special influence on the C–O bond in (I); there is a roughly parallel C–H bond on C(5), as is seen in Fig. 3(*b*), and carbonyl groups of neighbouring molecules oppose one another across the centre of symmetry at $\frac{1}{2}$, 0, $\frac{1}{2}$, in anti-parallel arrangement, as shown in Fig. 2; the possibility of hydrogen bonding has already been indicated. (This bonding is to a different molecule, related to the one shown by the centre of symmetry at $\frac{1}{2}$, 0, 0.)

The benzenoid ring is planar within experimental error, but C(4) lies out of this plane, in the direction of the oxygen atom, by about 0·1 Å, which appears to be significant. The bonds, C(1)–C(1′), C(1)–C(2), C(2)–C(3), C(3)–C(3′), and C(3)–C(4), are very similar in length, with values within the aromatic range. Only C(1)–C(2) is appreciably different, and the shortening of it has not more than possible significance. But it is noteworthy that the lengths found for all five bonds are extraordinarily similar to those occurring in analogous situations in the molecules of naphthalene, anthracene,[14] acridine,[15] and related compounds. Should this evidence be admitted, it provides further evidence in favour of unusual conjugation to the carbonyl group.

Very few measurements have yet been made of the dimensions of three-membered rings. Bastiansen and Hassel [16] found C–C = 1·54 Å from an electron-diffraction analysis of *cyclo*propane itself. In *spiro*pentane,[17] *cyclo*propyl chloride,[18] and *cyclo*propylidene dichloride [18] somewhat shorter values (1·48—1·52 Å) have been obtained by the same method. More exact results can be derived from micro-wave spectra, provided that sufficient isotopically substituted species are available; a study [19] of *cyclo*propyl chloride, though incomplete, led to C–C = 1·47 Å and indicated unequivocally that the C–C bond was shorter than a normal single bond. A similar length was found from the spectrum of ethylene oxide.[20] A *cyclo*propane ring system occurs in the molecule of Feist's acid; [21] and, according to Petersen's preliminary report [22] of a three-dimensional *X*-ray diffraction analysis, two of the bonds in the ring have C–C = 1·49, 1·50 Å, whilst the third, between the two carboxyl groups, has 1·55 Å. The experimental evidence is thus decidedly in favour of the view that this formally single bond is contracted. Coulson and Moffitt [23] have considered the structure of strained hydrocarbon rings in its theoretical aspect. For *cyclo*propane in particular they use the concept of " bent " bonds, and hence suggest an explanation of the paradox, that there is a diminution in the internuclear distance between carbon atoms, though—on the evidence of the force constant—the bond appears to be weakened.

In the present analysis, bond C(5)–C(6) is probably shorter than 1·54 Å. The length found for the other, non-equivalent, bond, C(5)–C(5′), exceeds 1·54 Å, but the difference is certainly not significant. On the other hand, that this bond may be significantly longer than C(5)–C(6) is just possible; and, if this be so, the difference is in the same sense as that in Feist's acid, and it can be readily attributed to the unusual conditions obtaining around this bond. The co-ordinates in Table 2 lead to an angle of 110° between the C–H bonds of the methylene group and to 124° for C(4)–C(5)–H, but these deviations from the tetrahedral angle are not significant.

[13] Josien, Fuson, Lebas, and Gregory, *J. Chem. Phys.*, 1953, **21**, 331.
[14] Cruickshank, *Acta Cryst.*, 1956, **9**, 915; 1957, **10**, 504.
[15] Phillips, *ibid.*, 1956, **9**, 248.
[16] Bastiansen and Hassel, cited in *Acta Chem. Scand.*, 1947, **1**, 156.
[17] Donohue, Humphrey, and Schomaker, *J. Amer. Chem. Soc.*, 1945, **67**, 332.
[18] O'Gorman and Schomaker, *ibid.*, 1946, **68**, 1138.
[19] Friend, Schneider, and Dailey, *J. Chem. Phys.*, 1955, **23**, 1557.
[20] Cunningham, Boyd, Myers, Gwinn, and Le Val, *ibid.*, 1951, **19**, 676.
[21] Lloyd, Downie, and Speakman, *Chem. and Ind.*, 1954, 222, 492
[22] Petersen, *ibid.*, 1956, 904.
[23] Coulson and Moffitt, *Phil. Mag.*, 1949, **40**, 1.

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The other bond-angles at the heavily stressed atom, C(5), are shown in Fig. 2. In connexion with the stereochemistry of this atom, certain dihedral angles are also relevant. These are represented in Fig. 3(*b*), which shows the relative directions and projected lengths of the adjacent bonds, as they appear when viewed along the C(5)–C(4) bond. The bonds (or, better, the interatomic vectors) from C(5) to C(5′), C(6) and H(5) are shown by the continuous lines; those from C(4) to O and C(3) by broken lines. The standard deviation in these dihedral angles is perhaps $\pm 2°$, except where the hydrogen atom is involved, when it will be considerably larger.

A feature of this molecule that was not wholly expected is that the methylene and phenylene groups are in a *cis*-configuration to one another, with respect to the intervening part of the molecule. [Small internal rotations about the two C(4)–C(5) bonds would lead to the *trans*-configuration.] A tentative explanation may be based on Fig. 3(*b*): the *cis*-configuration allows the bond C(4)–C(3) to take up an azimuthal position between the bonds C(5)–C(5′) and C(5)–C(6), and the polar bond C(4)–O to lie nearly in a plane with C(5)–H. The intermolecular contact described above may also help to settle the molecule in its conformation.

In discussing the situation at C(5), it is important to have reliable information about the position of H(5); and at present this is known only very roughly. Greater certainty on this point, as well as more precise knowledge of other details of this remarkable crystal structure, must wait on the three-dimensional study which it may be possible to undertake in due course.

Initial work on this structure in its *c*-axis projection was done by Dr. A. Vos during a brief visit to Glasgow under the auspices of the Netherlands Organisation for Pure Research (Z. W. O.). The authors thank Professor J. Monteath Robertson, F.R.S., for his interest, Imperial Chemical Industries Limited for supplying some of the equipment used, and the Department of Scientific and Industrial Research for financial support to W. K. G.

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768. *The Synthesis of 5-Iodotryptophan and Some Derivatives.*

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The synthesis of 5-iodotryptophan through 5-iodogramine is described.

DURING an investigation of antagonists of serotonin (5-hydroxytryptamine) consideration was given to the synthesis of 5-substituted indole and tryptophan derivatives with special emphasis on halogens. Several of these compounds have been reported, and Rydon and Tweddle [1] have described the four *Bz*-chloro-indoles and -tryptophans.

It was decided initially to attempt the synthesis of 5-iodotryptophan, as it might be possible to incorparate iodine-131 in a synthesis of the amino-acid later.

Preliminary experiments on ethyl *p*-iodophenylpyruvate hydrazone were unsatisfactory so attention was directed to the Reissert synthesis of indoles. 5-Iodo-2-nitrotoluene was condensed with ethyl oxalate, and the resulting potassium 2-iodo-5-nitrophenylpyruvate was reduced and cyclised to 5-iodoindole-2-carboxylic acid with ammoniacal ferrous hydroxide. Decarboxylation was accomplished by first removing all traces of sulphate [1] and then heating with copper chromite in quinoline. Yields of 5-iodoindole were consistently good.

Condensation of the indole with dimethylamine and formaldehyde in acetic acid yielded 5-iodogramine; this was condensed with diethyl formamidomalonate,[2] and the condensate

[1] Rydon and Tweddle, *J.*, 1955, 3499.
[2] Galat, *J. Amer. Chem. Soc.*, 1947, **69**, 965.

smoothly hydrolysed and decarboxylated to the 5-iodotryptophan. Condensation with acetaldehyde gave the tetrahydro-β-carbolinecarboxylic acid, which gave a typical " carboline " blue with ferric chloride in concentrated sulphuric acid and was oxidised to 8-iodo-2-methyl-β-carboline by acidic dichromate.

Biological tests for possible anti-serotonin effects will be published elsewhere, but it is interesting to note that the iodo-amino-acid has no significant effect on the oxygen consumption or on body weight of guinea-pigs.

Experimental

All m. p.s are uncorrected.

5-Iodo-2-nitrotoluene.—This was prepared from 5-amino-2-nitrotoluene [3] by Artmann's method.[4]

5-Iodo-2-nitrophenylpyruvic Acid and 5-Iodoindole-2-carboxylic Acid.—Preliminary experiments indicated that the best procedure for the formation of the indole was to reduce the alkaline extract of the Reissert condensation without isolation of the 2-nitrophenylpyruvic acid.[5] Ethyl oxalate (30 g.) in benzene (100 ml.) was added (15 min.) below 15° to potassium ethoxide solution [from potassium (7·5 g.), dry ethanol (75 ml.) and benzene (350 ml.)], followed by 5-iodo-2-nitrotoluene (50 g.) in benzene (100 ml.). The solution was refluxed for 0·5 hr. and while still hot extracted with potassium hydroxide solution (5% w/v; 750 ml.) and with water (250 ml.). 5-Iodo-2-nitrotoluene (25 g.) was recovered from the benzene.

A part (100 ml.) of the alkaline extract was acidified to pH 1 (10N-hydrochloric acid at 0°) and extracted with ether (100 ml.). The ether was extracted with sodium hydroxide (5% w/v; 100 ml.), clarified (charcoal; 80°), cooled to 0°, and acidified as before. The *acid* formed sandy-yellow needles (2 g., 32% based on 5 g. of nitrotoluene), m. p. 134° (from benzene) (Found: C, 32·7; H, 1·9; N, 4·4. $C_9H_6O_3NI$ requires C, 32·2; H, 1·8; N, 4·1%).

The remainder (900 ml.) of the alkaline extract was added with stirring to a suspension of alkaline ferrous hydroxide [heptahydrate (150 g.), water (750 ml.), and ammonia (*d* 0·88; 90 ml.)]. The mixture was boiled (10 min.) and filtered, and the filtrate boiled with dilute ammonia solution (5% v/v; 3 × 500 ml.). The combined filtrates were cooled and acidified to pH 1 (10N-hydrochloric acid), and the precipitate extracted with ether. The ether extracts were washed with water, barium chloride solution (0·5% w/v; 250 ml.), and again with water. On concentration the *indole* separated (15 g., 30% based on 45 g. of nitrotoluene); it formed hexagons, m. p. 248—250° (decomp.), from ethanol (Found: C, 37·5; H, 2·2; N, 5·2. $C_9H_6O_2NI$ requires C, 37·6; H, 2·1; N, 4·9%).

5-Iodoindole.—The crude, dry sulphate-free indole acid (20 g.) was ground with copper chromite [6] (2·0 g.), and the mixture in redistilled quinoline (50 ml.) gently refluxed for 2·0 hr. The mixture was poured into water, acidified (2N-hydrochloric acid), and extracted with ether. The ethereal extract was washed successively with 2N-hydrochloric acid, 2N-sodium hydrogen carbonate, and distilled water, dried (Na_2SO_4), and evaporated to give the crude indole (6·5 g., 64%) which was pure enough for preparation of the gramine. A portion twice recrystallized from aqueous methanol (charcoal) formed silvery plates, m. p. 99° (Found: C, 39·4; H, 2·5; N, 5·8. C_8H_6NI requires C, 39·5; H, 2·5; N, 5·8%).

3-Dimethylaminomethyl-5-iodoindole (*5-Iodogramine*).—Acetic acid (0·6 ml.) was added at 0—4° to a solution of dimethylamine (26% w/v; 0·7 ml.); this was followed by formaldehyde (36% w/v; 0·28 ml.), and the mixture poured on 5-iodoindole (1·22 g.). After 6 hr. at room temperature the solution was poured into sodium hydroxide (10 ml.; 2·5 N) and extracted with ether. The extract was washed with dilute alkali and then water, and extracted with 2N-hydrochloric acid. The acid was clarified (charcoal) and treated with a slight excess of dilute ammonia solution (10% v/v); *3-dimethylaminomethyl-5-iodoindole* was precipitated (0·72 g., 48%), and formed rectangles, m. p. 159°, from aqueous methanol (Found: C, 43·2; H, 4·4; N, 8·7. $C_{11}H_{13}N_2I$ requires C, 44·0; H, 4·3; N, 9·3%).

Diethyl α-Formamido-α-(5-iodo-3-indolylmethyl)malonate.—A mixture of 5-iodogramine

[3] Cohen and Dakin, *J.*, 1910, 321.
[4] Artmann, *Monatsh.*, 1905, **26**, 1091.
[5] Cf. Allen, Brunton, and Suschitzky, *J.*, 1955, 1283.
[6] Vogel, " Practical Organic Chemistry," Longmans, Green & Co., London, 2nd edn., 1951, p. 808.

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(1·64 g.) and diethyl formamidomalonate (1·5 g.) was added to boiling toluene (5·0 ml.) containing sodium hydroxide (0·2 g.), and the mixture gently refluxed (0·5 hr.). The cooled mixture was treated with light petroleum (5 ml.; b. p. 40—60°), the solvents were decanted off, and ice-water (10 ml.) and ether (10 ml.) added to the residue. The ether extract was washed with water, dried (Na_2SO_4), and concentrated to yield *diethyl α-formamido-α-(5-iodo-3-indolylmethyl)malonate* (1·6 g., 64%), which formed stout rhombs, m. p. 156°, from aqueous methanol (Found: C, 45·4; H, 4·3; N, 6·2. $C_{17}H_{19}O_5N_2I$ requires C, 44·5; H, 4·1; N, 6·1%).

Diethyl α-Acetamido-α-(5-iodo-3-indolylmethyl)malonate.—Diethyl acetamidomalonate (0·7 g.) was added with shaking and cooling (ice) to sodium ethoxide [sodium (0·6 g.) and anhydrous ethanol (5·0 ml.)]. This was followed by 5-iodogramine (0·72 g.) and dimethyl sulphate (0·44 g.). The temperature was maintained at 40° for 6·0 hr. then at room temperature for 18 hr. Thereafter water (20 ml.) was added. *Diethyl α-acetamido-α-(5-iodo-3-indolylmethyl)malonate* crystallised (0·93 g., 82%), and formed cubes, m. p. 160°, from aqueous methanol (Found: C, 45·3; H, 4·3; N, 5·6. $C_{18}H_{21}O_5N_2I$ requires C, 45·7; H, 4·4; N, 5·9%).

5-Iodotryptophan.—Diethyl α-formamido-α-(5-iodo-2-indolylmethyl)malonate (1·0 g.), aqueous sodium hydroxide (2·5N; 8·0 ml.), and ethanol (2·0 ml.) were refluxed for 0·5 hr., the ethanol then distilled off, and refluxing continued for 5·0 hr. (charcoal). Acetic acid (1·0 ml.) was added and the solution refluxed for 1·0 hr. and then set aside overnight. 5-Iodotryptophan (0·55 g., 76%) formed rosettes from dilute ammonia solution or leaflets from glacial acetic acid that darkened at 250° and had m. p. 264° (Found: C, 38·8; H, 4·1; N, 7·6. $C_{11}H_{11}O_2N_2I,2H_2O$ requires C, 36·0; H, 4·1; N, 7·6%).

On mixing a dilute solution of the amino-acid with glyoxylic acid and underlayering it with concentrated sulphuric acid, an intense purple upper band and a blue-green lower band were formed. With dilute formaldehyde underlayered with sulphuric acid, an upper yellow orange band and a faint purple lower band were formed. A trace of ferric chloride made the bands almost black.

Attempted hydrolysis and decarboxylation of the acetamido-compound by refluxing it in 1·5N-hydrochloric acid were unsatisfactory and an increase in the strength of the acid caused marked decomposition.

2 : 3 : 4 : 5-Tetrahydro-8-iodo-2-methyl-β-carboline-4-carboxylic Acid.—5-Iodotryptophan (0·1 g.) in sulphuric acid (0·1N; 10 ml.) and aqueous acetaldehyde (10% w/v; 2·5 ml.) were maintained at 40° for 18 hr. The mixture was boiled, clarified (charcoal), and made alkaline (10% w/v ammonia). The *carbolinecarboxylic acid* (0·08 g., 75%) formed blunt, colourless rods, m. p. 277°, from dilute ammonia, and gave a typical "carboline blue" colour [7] with concentrated sulphuric acid and a trace of ferric chloride (Found: C, 40·7; H, 4·3; N, 7·3. $C_{13}H_{13}O_2N_2I,2H_2O$ requires C, 39·7; H, 4·3; N, 7·1%).

8-Iodo-2-methyl-β-carboline.—The clarified solution from the reaction of 5-iodotryptophan, acid, and acetaldehyde (previous experiment) was boiled with potassium dichromate (10 w/v; 5·0 ml.) and acetic acid (1·0 ml.) for 3 min. Aqueous sodium sulphite (saturated; 5·0 ml.) and aqueous sodium carbonate (saturated; 5·0 ml.) were added, and the mixture extracted with ether. The dried (Na_2SO_4) extract yielded pale brown crystals (40 mg.; 43%) that formed very pale brown tablets, m. p. 216°, from methanol (Found: C, 46·6; H, 2·9; N, 9·2%. $C_{12}H_9N_2I$ requires C, 46·7; H, 2·9; N, 9·1%).

I am indebted to Professor H. N. Rydon for suggestions.

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Royal Veterinary College, London, N.W.1. [*Received, March 20th*, 1958.]

[7] Cf. Miller, Harvey, and Robson, *J.*, 1940, 153; Marchant and Harvey, *J.*, 1951, 1808.

769. *Structure and Properties of Mesomeric Systems. Part IV.* The Chemical Reactivity of Non-alternant Aza-heterocycles.*

By David Peters.

A perturbation method, based on the Hückel L.C.A.O. molecular-orbital theory, is used to predict that replacement of a carbon atom in a $(4\gamma + 2)$ non-alternant hydrocarbon by a nitrogen atom will have little or no effect on the orientation of ionic substitution in the molecule.

The Hückel L.C.A.O. molecular-orbital theory [1] has had much success in interpreting the chemistry of benzenoid hydrocarbons [2] owing partly to the development of perturbation methods [2b,c] which eliminate the heavy labour involved in the formal calculations. The non-alternant hydrocarbons are now receiving much attention,[2a,3] but theoretical interpretation of their chemistry has, until recently, been hampered because the available perturbation methods are not generally applicable to them. This difficulty was overcome for many of this class by the development of alternative perturbation methods which are capable of dealing with both classes of hydrocarbon.[4] Thus the theory of the chemistry of many of the non-alternant hydrocarbons is now as easily discussed as is that of the alternant ones. The new method is based on the idea [5] that the properties of aromatic systems can be deduced from those of the corresponding cyclic polyene, the formation of the cross-links being treated as a perturbation. Thus azulene is formally obtained from *cyclo*decapentaene by cross-linking (see *J.*, 1958, 1040).

The properties of the Wheland [6] transition state can similarly be obtained from those of the corresponding open-chain polyene radical or ion. In this way, the charge distributions and localisation energies of many of the non-alternant hydrocarbons are easily obtained.[4]

We now attempt to develop these ideas further, applying them first to the replacement of a carbon atom of the mesomeric hydrocarbon by a nitrogen atom, forming a non-alternant heterocycle, and secondly to the introduction of a substituent into the hydrocarbon. The formal method of handling the first case, the aza-heterocycles, is to assign to the nitrogen atom a Coulomb integral differing from that of a carbon atom and solve the resulting secular equations.[7] For the larger hydrocarbons, however, the solution of these equations is prohibitively long, and perturbation methods are commonly employed.[8] It is then supposed that the variation of the Coulomb integral may be taken as a perturbation. This method is used here.

Substituent effects are more difficult to deal with, our general understanding of their action being far from perfect. In the following paper we divide substituent action into two effects, inductive and mesomeric; the former will be dealt with in the same way as

* Part III, *J.*, 1958, 1039.

[1] Hückel, *Z. Physik*, 1930, **60**, 423; 1931, **70**, 204; 1931, **72**, 310; 1932, **76**, 628.

[2] (*a*) Pullman and Pullman, "Les Theories Electroniques de la Chimie Organique," Masson et Cie., Paris, 1952; (*b*) Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39; 1947, *A*, **192**, 16; (*c*) Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3355.

[3] Baker and McOmie, "Progress in Organic Chemistry," Butterworths Scientific Publications London, 1955, vol. 3, p. 44.

[4] Peters, *J.*, 1958, 1023, 1028, 1039.

[5] (*a*) Platt, *J. Chem. Phys.*, 1949, **17**, 484; (*b*) Dewar and Pettit, *J.*, 1954, 1617.

[6] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.

[7] (*a*) Davies, *Trans. Faraday Soc.*, 1955, **51**, 449; Burr, *J. Chem. Phys.*, 1957, **26**, 431; (*b*) Wheland and Pauling, *J. Amer. Chem. Soc.*, 1935, **57**, 2086; Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, 1947, **43**, 87; Orgel, Cottrell, Dick, and Sutton, *ibid.*, 1951, **47**, 113; Nordheim and Sponer, *J. Chem. Phys.*, 1952, **20**, 285; Brown, *J.*, 1956, 272; Gyoerffy, *Compt. rend.*, 1951, **232**, 515; Chalvet and Sandorfy, *ibid.*, 1949, **228**, 566; Sandorfy, *Bull. Soc. chim. France*, 1949, **16**, 615.

[8] (*a*) Coulson and Longuet-Higgins, *J.*, 1949, 971; Jaffé, *J. Chem. Phys.*, 1952, **20**, 1554 Löwdin, *ibid.*, 1951, **19**, 1323. (*b*) Dewar and Maitlas, *J.*, 1957, 2521; Sandorfy and Yvan, *Bull. Soc. chim. France*, 1950, **17**, 131.

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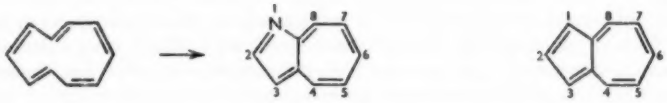
the introduction of the nitrogen atom, so that the methods used here can be carried over immediately for it.

We examine the influence on the chemistry of a $(4\gamma + 2)$ non-alternant hydrocarbon of changing the Coulomb integral of one of the carbon atoms. We will be concerned largely with the aza-heterocycles derived from azulene (a useful model) although some of the larger $(4\gamma + 2)$ non-alternant hydrocarbons will be discussed briefly. No attempt is made to deal with the (4γ) non-alternant hydrocarbons, there being so little evidence against which the theory can be checked. As an example, we regard 1-aza-azulene as being formed from *cyclo*decapentaene by cross-linking and introduction of the nitrogen atom:



Method.—The two main theories of chemical reactivity, the isolated-molecule and the localisation approximations [9] are used. In the former, it is supposed that the charge distribution in the ground state determines the position of ionic attack, the atom having the largest surplus of negative (positive) charge being the preferred position of electrophilic (nucleophilic) attack. In the latter, the energies of the ground and the transition state are calculated, the difference being the activation energy. The transition state is taken [6] as the ground state with the atom undergoing substitution removed from the mesomeric system and the usual assumption is made that the π-electron energy is the only part of the activation energy to vary with the structure of the substrate. Full details of both methods have been set out elsewhere.[9] Overlap is neglected since its inclusion usually makes only minor differences.[7a,10]

The Isolated-molecule Approximation.—Here we require the charge distribution in the ground state of the cross-linked, nitrogen-substituted, cyclic polyene. This differs from that in the cyclic polyene itself by the effects of the two perturbations. First-order perturbations being additive, we write:

$$q_t' = q_t + (\partial q_t/\partial\beta_{rs})\delta\beta_{rs} + (\partial q_t/\partial\alpha_p)\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where q_t is the charge on atom t, $\delta\beta_{rs}$ is the change in the resonance integral * of the bond between atoms r and s and $\delta\alpha_p$ is the change in the Coulomb integral * of atom p. Higher-order terms, including the first cross product, are neglected. Coulson and Longuet-Higgins's nomenclature being followed,[2b]

$$\partial q_t/\partial\beta_{rs} = \pi_{t,rs} \text{ and } \partial q_t/\partial\alpha_p = \pi_{t,p}$$

or

$$q_t' = 1 + \pi_{t,rs}\,.\,\delta\beta_{rs} + \pi_{t,p}\,.\,\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\pi_{r,rs}$ and $\pi_{t,p}$ are the atom–bond and the atom–atom polarisabilities respectively. The charge distribution in the cyclic polyene itself is, of course, unity ($q_t = 1$). If there are several cross-links and several atoms whose Coulomb integrals differ from that of a carbon atom, we have:

$$q_t' = 1 + \sum_{rs}\pi_{t,rs}\,.\,\delta\beta_{rs} + \sum_{p}\pi_{t,p}\,.\,\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad (2a)$$

These authors show that we may use these formulæ for the doubly-degenerate molecular-orbitals of the cyclic polyenes providing we use the correct zeroth-order molecular-orbitals.

* The resonance integral β_{rs} is defined as $\int\phi_r H\phi_s d\tau$, the Coulomb integral α_p as $\int\phi_p H\phi_p d\tau$ where the ϕ's are carbon $2p$-atomic orbitals and H is the effective one-electron Hamiltonian.

[9] R. D. Brown, *Quart. Rev.*, 1952, **6**, 63.
[10] Chirgwin and Coulson, *Proc. Roy. Soc.*, 1950, *A*, **201**, 196; de Heer, *Phil. Mag.*, 1950, **41**, 370.

When $\delta\alpha_p$ is zero, we have the effect of the cross-linking alone on the charge distribution of the cyclic polyene. This has been evaluated in Part III, where a number of examples were discussed. When $\delta\beta_{rs}$ is zero, we have the effect of the change in Coulomb integral on the charge distribution of the cyclic polyene. The polarisability $\pi_{t,p}$ is given [2b] by

$$\pi_{t,p} = 4 \sum_{j=1}^{m} \sum_{k=m+1}^{n} \frac{c_{jp} \cdot c_{jt} \cdot c_{kp} \cdot c_{kt}}{(e_j - e_k)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where the bonding molecular-orbitals are $1 - m$, the antibonding are $(m + 1) - n$, e_j, and e_k are the energies of the jth and kth molecular-orbitals respectively and the c's are atomic-orbital coefficients whose nomenclature is derived from that of the other quantities. This expression reduces (Appendix) to

$$\pi_{t,p} = 4 \cos(t-p)\pi \left[\sum_{j=0}^{\gamma} \frac{\chi_j^4}{2e_j} \cos^2 \left\{ 2(t-p)j\frac{\pi}{n} \right\} + 2 \sum_{j=0}^{\gamma-1} \sum_{h=j+1}^{\gamma} \frac{\chi_j^2 \chi_h^2}{e_j + e_h} \cos 2(t-p)j\frac{\pi}{n} \cdot \cos 2(t-p)h\frac{\pi}{n} \right] \quad . \quad (4)$$

where h is the bonding molecular-orbital conjugated with k. The χ's are defined below. From eqn. (4), the atom–atom polarisabilities given in Table 1 are calculated and, combining these with the atom–bond polarisabilities given in Part III, we calculated the total charge distributions in Table 2 from eqn. (2).

The Localisation Approximation.—Here we require the π-electron energy of the ground and the transition state. Taking the cyclic polyene as starting point, we need the total change in its π-electron energy ($\delta E_{\text{c.p.}}$) resulting from the change in the resonance integral ($\delta\beta_{rs}$) of the bond between atoms r and s and the change in Coulomb integral ($\delta\alpha_p$) of atom p. Expanding the π-electron energy of the cyclic polyene as a function of these two perturbations we obtain

$$\delta E_{\text{c.p.}} = (\partial E_{\text{c.p.}}/\partial\beta_{rs})\delta\beta_{rs} + (\partial E_{\text{c.p.}}/\partial\alpha_p)\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad (5)$$

to the first approximation. Higher terms, including the first cross product, are neglected and the two perturbations are additive. The change ($\delta E_{\text{p.r.}}$) in the π-electron energy of the polyene radical ($E_{\text{p.r.}}$) under the same two perturbations is similarly

$$\delta E_{\text{p.r.}} = (\partial E_{\text{p.r.}}/\partial\beta_{rs})\delta\beta_{rs} + (\partial E_{\text{p.r.}}/\partial\alpha_p)\delta\alpha_p \quad . \quad . \quad . \quad . \quad (6)$$

The atom localisation energies for free-radical substitution ($\mathscr{E}_{\text{h}}$) in the cross-linked, nitrogen-substituted cyclic polyene are then

$$\mathscr{E}_{\text{h}} = E_{\text{c.p.}} + \delta E_{\text{c.p.}} - E_{\text{p.r.}} - \delta E_{\text{p.r.}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$\mathscr{E}_{\text{h}} = [E_{\text{c.p.}} + (\partial E_{\text{c.p.}}/\partial\beta_{rs})\delta\beta_{rs} + (\partial E_{\text{c.p.}}/\partial\alpha_p)\delta\alpha_p] - [E_{\text{p.r.}} + (\partial E_{\text{p.r.}}/\partial\beta_{rs})\delta\beta_{rs} + (\delta E_{\text{p.r.}}/\delta\alpha_p)\delta\alpha_p] \quad . \quad . \quad . \quad (8)$$

But from Part II (eqn. 1):

$$\mathscr{E}_{\text{a}} = [E_{\text{c.p.}} + (\partial E_{\text{c.p.}}/\partial\beta_{rs})\delta\beta_{rs}] - [E_{\text{p.r.}} + (\partial E_{\text{p.r.}}/\partial\beta_{rs})\delta\beta_{rs}] \quad . \quad . \quad (9)$$

where $\mathscr{E}_{\text{a}}$ is the atom localisation energy for free-radical substitution in the cross-linked hydrocarbon. Hence

$$\mathscr{E}_{\text{h}} = \mathscr{E}_{\text{a}} + [(\partial E_{\text{c.p.}}/\partial\alpha_p) - (\partial E_{\text{p.r.}}/\partial\alpha_p)]\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad (10)$$

It remains to evaluate the two terms in the bracket in eqn. (10). The second of these is immediately given, in free-radical substitution, by

$$\delta E_{\text{p.r.}}/\delta\alpha_p = q_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

To evaluate the first, the first-order perturbation of degenerate systems must be considered.

With the exception of the lowest bonding and the highest anti-bonding, the molecular-orbitals [ψ(cos),ψ(sin)] of the cyclic polyene (C_nH_n) occur in doubly-degenerate pairs

$$\left.\begin{aligned}\psi_j\,(\cos) &= \sum_{a=1}^{n} \chi_j \cos\left[\left(2aj\frac{\pi}{n}\right)+\zeta_j\right]\phi_a \\ \psi_j\,(\sin) &= \sum_{a=1}^{n} \chi_j \sin\left[\left(2aj\frac{\pi}{n}\right)+\zeta_j\right]\phi_a\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (12)$$

where χ_j is the normalising factor, equal to $(1/n)^{\frac{1}{2}}$ for the non-degenerate orbitals and to $(2/n)^{\frac{1}{2}}$ for the doubly-degenerate; ϕ_a is a carbon $2p$-atomic orbital; j is a quantum number and ζ is a phase factor chosen arbitrarily in the cyclic polyenes themselves. The perturbation, the change in the Hamiltonian operator, being denoted by H′, the usual second-order determinant is

$$\begin{vmatrix} H_{11}^{(1)} - \delta e_j & H_{12}^{(1)} \\ H_{21}^{(1)} & H_{22}^{(1)} - \delta e_j \end{vmatrix} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

where $H_{11}^{(1)} = \int \psi_j\,(\sin)\, H'\psi_j\,(\sin)\,d\tau \qquad H_{22}^{(1)} = \int \psi_j\,(\cos)\, H'\psi_j\,(\cos)\,d\tau$

$$H_{12}^{(1)} = H_{21}^{(1)} = \int \psi_j\,(\sin)\, H'\psi_j\,(\cos)\,d\tau$$

and δe_j is the first-order correction to the energy of the jth molecular-orbital. Now by Dewar and Pettit's method,[5b] the secular determinant can be solved and the phase factor ζ determined by choosing ζ so that the off-diagonal elements $H_{12}^{(1)}$ vanish:

$$H_{12}^{(1)} = \int \sum_{a=1}^{n} \chi_j \cos\left[\left(2aj\frac{\pi}{n}\right)+\zeta_j\right] \sum_{a=1}^{n} \sin\left[\left(2aj\frac{\pi}{n}\right)+\zeta_j\right]\phi_a H'\phi_a d\tau = 0 \quad . \quad (14)$$

If the only non-vanishing matrix element is $\int \phi_p H'_p d\tau = \delta\alpha_p$, we have

$$\cos\left(2pj\frac{\pi}{n}+\zeta_j\right).\sin\left(2pj\frac{\pi}{n}+\zeta_j\right).\delta\alpha_p = 0 \quad . \quad . \quad . \quad . \quad . \quad (15)$$

$$\sin\left(4pj\frac{\pi}{n}+2\zeta_j\right) = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16)$$

$$\sin\left(4pj\frac{\pi}{n}\right).\cos(2\zeta_j) + \cos\left(4pj\frac{\pi}{n}\right).\sin(2\zeta_j) = 0 \quad . \quad . \quad . \quad . \quad (17)$$

$$\tan(2\zeta_j) = -\tan\left(4pj\frac{\pi}{n}\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

whose primitive solution is

$$\zeta_j = 2\,pj\pi/n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (19)$$

For several cross-links, ζ is given by

$$\tan\,(2\zeta) = -\sum \sin\,(4pj\pi/n)/\sum \cos\,(4pj\pi/n) \quad . \quad . \quad . \quad . \quad . \quad (20)$$

the summations being taken over the cross-links. The energies of the perturbed molecular-orbitals are

$$\delta e_j\,(\sin) = \int \psi_j\,(\sin)\, H'\psi_j\,(\sin)\,d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad (21)$$

$$= \sum_{a=1}^{n}\sum_{a=1}^{n} \chi_j^2 \sin^2\left(2aj\frac{\pi}{n}+\zeta_j\right).\delta\alpha_a \quad . \quad . \quad . \quad (22)$$

$$= \chi_j^2 \sin^2\left(2pj\frac{\pi}{n}+\zeta_j\right)\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad . \quad (23)$$

and

$$\delta e_j\,(\cos) = \chi_j^2 \cos^2\left(2pj\frac{\pi}{n}+\zeta_j\right)\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad (24)$$

Equations (23) and (24) confirm that the degeneracy does not affect the result, since for non-degenerate molecular-orbitals we have immediately

$$\delta\epsilon_j = c_{jp}^2 . \delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (25)$$

Accordingly, we can write

$$\delta E_{\text{c.p.}}/\delta\alpha_p = q_p = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (26)$$

the charge density in the cyclic polyene being unity. In free-radical substitution, the charge density in the polyene radical is also unity, so that from equations (10), (11), and (26)

$$\mathscr{E}_{\text{h}} = \mathscr{E}_{\text{a}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (27)$$

Replacement of a carbon atom in a non-alternant hydrocarbon by a nitrogen atom thus has no effect on the free-radical reactivity. No doubt this conclusion oversimplifies the true position, but it shows that in the non-alternant hydrocarbons, as in benzene,[11] free-radical reactivity is only slightly affected by the introduction of a nitrogen atom.

It is in ionic reactivity that the effect of the nitrogen atom is more pronounced, both in the alternant and in the non-alternant systems. In this case, the non-bonding molecular-orbital of the polyene radical is no longer singly occupied but is doubly occupied (nucleophilic) or is unoccupied (electrophilic). The resulting modification of the localisation energies of the cross-linked hydrocarbon has been dealt with in Part II. The charge on atom p in the polyene radical is given by

$$q_p = (1 + c_{op}^2) = \delta E_{\text{p.r.}}/\delta\alpha_p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (28)$$

where c_{op} is the coefficient at atom p of the non-bonding molecular-orbital of the polyene radical. The minus sign is taken in electrophilic, and the plus sign in nucleophilic, substitution. Now the non-bonding molecular-orbital coefficients are immediately given [12] by

$$\sum_s c_{op} . \beta_{rs} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (29)$$

followed by normalisation. The summation in equation (29) is over all atoms (s) adjacent to atom r. The resonance integral β_{rs} is taken as the standard resonance integral β. The ionic localisation energies are then from eqn. (10)

$$\mathscr{E}_{\text{h}}^{+} = \mathscr{E}_{\text{a}}^{+} + [1 - (1 - c_{op}^2)]\delta\alpha_p = \mathscr{E}_{\text{a}}^{+} + c_{op}^2 . \delta\alpha_p \quad . \quad . \quad . \quad (30)$$

$$\mathscr{E}_{\text{h}}^{-} = \mathscr{E}_{\text{a}}^{-} + [1 - (1 + c_{op}^2)]\delta\alpha_p = \mathscr{E}_{\text{a}}^{-} - c_{op}^2 . \delta\alpha_p \quad . \quad . \quad . \quad (31)$$

The localisation energies $\mathscr{E}_{\text{h}}^{+}$ and $\mathscr{E}_{\text{h}}^{-}$ refer to electrophilic and to nucleophilic attack respectively; $\mathscr{E}_{\text{a}}^{+}$ and $\mathscr{E}_{\text{a}}^{-}$ are the same quantities in the parent hydrocarbon. From eqns. (30) and (31) and the values of $\mathscr{E}_{\text{a}}^{+}$ and $\mathscr{E}_{\text{a}}^{-}$ given in Part II, the results reported in Table 2 are calculated.

As in all work of this kind, there remains the problem of the numerical value of the Coulomb integral of the nitrogen atom (α_{N}). If we write $\alpha_{\text{N}} = \alpha_{\text{C}} + h\beta$ or $\delta\alpha_{\text{N}} = h\beta$, we must assign a value to the parameter h. The sum of experience so far[7,8,13] suggests that h is in the range $+0{\cdot}5$ to $+1{\cdot}0$, but slightly different values will no doubt be required in different situations to absorb the error inherent in the Hückel method. Fortunately the exact value of h in this range is not critical for this work, and we have taken $h = 1{\cdot}0$ to avoid underestimating the effect of the nitrogen atom. It is also necessary to allow for the change in the Coulomb integral (α_{C}') of the carbon atoms adjacent to the nitrogen atom. This is the so-called σ inductive effect. We write $\alpha_{\text{C}}' = \alpha_{\text{C}} + k\beta$ and take k as

[11] Hey and Williams, *Discuss. Faraday Soc.*, 1953, **14**, 216.
[12] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.
[13] R. D. Brown and Penfold, *Trans. Faraday Soc.*, 1957, **53**, 397.

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1/3.[8b,14] Only immediate neighbours are considered, and again the results do not depend critically on the choice of this parameter. The resonance integral of the bond between a a carbon and a nitrogen atom is taken as $1{\cdot}0\beta$.

Results.—The atom–atom polarisabilities ($\pi_{t,p}$) for the 10- and the 14-atom cyclic polyenes are recorded in Table 1. In Table 2, the charge distributions and localisation energies for the aza-azulenes are reported. The figures for azulene itself are taken from Parts II and III.

TABLE 1.

$C_{10}H_{10}$	$\pi_{1,1}$ +0·437	$\pi_{1,2}$ −0·145	$\pi_{1,3}$ +0·028	$\pi_{1,4}$ −0·072	$\pi_{1,5}$ +0·002	$\pi_{1,6}$ −0·063		
$C_{14}H_{14}$	$\pi_{1,1}$ +0·455	$\pi_{1,2}$ −0·141	$\pi_{1,3}$ +0·039	$\pi_{1,4}$ −0·063	$\pi_{1,5}$ +0·008	$\pi_{1,6}$ −0·048	$\pi_{1,7}$ +0·001	$\pi_{1,8}$ −0·045

TABLE 2. *Distribution of charge* $(1 - q_t)$ *and ionic localisation energies* ($\mathscr{E}_h^+$, $\mathscr{E}_h^-$) *(in units of* β*) of azulene and the aza-azulenes. For this paper we revert to standard chemical numbering as shown on p.* 3764.

Atom (t)	1	2	3	4	5	6	7	8
Charge ...	−0·185	−0·056	−0·185	+0·163	+0·015	+0·144	+0·015	+0·163
$\mathscr{E}_h^+$	1·92	2·32	1·92	2·72	2·32	2·72	2·32	2·72
$\mathscr{E}_h^-$	2·72	2·32	2·72	1·92	2·32	1·92	2·32	1·92
Charge ...	**N**	−0·065	−0·141	+0·206	+0·077	+0·187	+0·077	+0·206
Charge	**N**	*+0·069*	*−0·151*	*+0·145*	*+0·055*	*+0·130*	*+0·061*	*+0·168*
$\mathscr{E}_h^+$	**N**	2·52	2·06	2·86	2·52	2·86	2·52	2·86
$\mathscr{E}_h^-$	**N**	2·12	2·58	1·78	2·12	1·78	2·12	1·78
Charge ...	−0·194	**N**	−0·194	+0·225	+0·058	+0·206	+0·058	+0·225
Charge	*−0·038*	**N**	*−0·038*	*+0·186*	*+0·013*	*+0·168*	*+0·013*	*+0·186*
$\mathscr{E}_h^+$	2·12	**N**	2·12	2·92	2·46	2·92	2·46	2·92
$\mathscr{E}_h^-$	2·52	**N**	2·52	1·72	2·18	1·72	2·18	1·72
Charge ...	−0·142	+0·006	−0·141	**N**	+0·006	+0·188	+0·077	+0·206
$\mathscr{E}_h^+$	2·06	2·52	2·06	**N**	2·52	2·86	2·52	2·86
$\mathscr{E}_h^-$	2·58	2·12	2·58	**N**	2·12	1·78	2·12	1·78
Charge ...	−0·124	−0·013	−0·123	+0·154	**N**	+0·135	+0·059	+0·225
$\mathscr{E}_h^+$	2·12	2·46	2·12	2·92	**N**	2·92	2·46	2·92
$\mathscr{E}_h^-$	2·52	2·18	2·52	1·72	**N**	1·72	2·18	1·72
Charge ...	−0·142	+0·006	−0·142	+0·207	+0·006	**N**	+0·006	+0·207
Charge	*−0·173*	*+0·005*	*−0·173*	*+0·133*	*+0·155*	**N**	*+0·155*	*+0·133*
$\mathscr{E}_h^+$	2·06	2·52	2·06	2·86	2·52	**N**	2·52	2·86
$\mathscr{E}_h^-$	2·58	2·12	2·58	1·78	2·12	**N**	2·12	1·78

DISCUSSION

Kon [15] has solved the secular equations for 1-, 2-, and 6-aza-azulene, taking $h = 1$ as in the present paper, but neglecting the σ inductive effect—*i.e.*, taking $k = 0$. The resulting charge distribution is given in *italics* in Table 2. The agreement between these figures and the present results is good, except for the positions adjacent to the nitrogen atoms and here Kon's neglect * of the σ inductive effect must give too low a charge density. Further theoretical data on the charge distribution or localisation energies of the aza-azulenes are not available, and there is little experimental evidence against which the theory can be checked, although 1-aza-azulene has been prepared [16] and several derivatives of the aza-azulenes are known.[17,18]

In the results of the perturbation method, there is generally good agreement between the two methods of predicting the chemical reactivity and this agreement reinforces our confidence in these predictions. The charge distribution and localisation energies in

* In his " correction 1."

[14] Jaffé, *J. Chem. Phys.*, 1953, **21**, 415.
[15] Kon, *Sci. Reports Tohoku Univ.*, 1954, **38**, 67.
[16] Nozoe, Seto, Matsumura, Terasawa, *Chem. and Ind.*, 1954, 1357.
[17] Treibs, *Annalen*, 1952, **576**, 110; Treibs, Steinert, and Kirchhof, *ibid.*, 1953, **581**, 54; Anderson and Tazuma, *J. Amer. Chem. Soc.*, 1952, **74**, 3455; Lloyd, *Chem. and Ind.*, 1953, 921; Hunter, Lloyd, Marshall, Price, and Rowe, *ibid.*, 1954, 1068.
[18] Nozoe, Mukai, and Murata, *J. Amer. Chem. Soc.*, 1954, **76**, 3352.

Table 2 immediately establish the important point that, insofar as ionic substitution is concerned, the chemistry of azulene is qualitatively unaffected by the introduction of the nitrogen atom. That is, the predicted orientation of ionic attack is the same in the heterocycle as in the parent hydrocarbon, and this result is quite different from that in the alternant systems.[8b] The effect of the nitrogen atom is the same, in this approximation, in both classes of hydrocarbon, but the large variations in reactivity between the different positions in the non-alternant systems mask the directive effect of the nitrogen atom. It is clear from Table 2 that a very unreasonable choice of h or k would be required to invalidate this conclusion.

While the orientation of ionic attack should be the same in the heterocycle as in the parent hydrocarbon, the rate of attack will, of course, be affected but one cannot be certain that the crude perturbation method will correctly predict this more subtle effect. It is clear from the figures that all the aza-azulenes differ from azulene itself in much the same way. The effect of the nitrogen atom in all but one of the aza-azulenes is to reduce the electron surplus on atoms 1 and 3 and to increase the electron deficit on 4, 6, and 8. Furthermore, the electrophilic localisation energies of the 1- and the 3-position are increased while the nucleophilic localisation energies of atoms 4, 6, and 8 are reduced. So if the perturbation method is sufficiently accurate for this purpose, we may expect, in general, reduced electrophilic reactivity in positions 1 and 3 and increased nucleophilic reactivity at positions 4, 6, and 8. There is a little confirmatory evidence here, 1 : 3-diaza-azulene being resistant to electrophilic attack.[18]

The general conclusion requires qualification. First, the nitrogen atom will have its own intrinsic properties—protonation, quaternisation, etc. Secondly, the assumption of the Wheland transition state is apparently not valid for all processes which might be expected to be electrophilic substitutions.[19] Thirdly, the true transition state occurs earlier in the molecular act than the point represented by the Wheland transition state.[8b] Fourthly, there is not complete quantitative agreement between the localisation and the static methods, but this is commonly the case in the non-alternant systems.[20] Fifthly, in electrophilic substitution in acid media, the nitrogen atom is protonated and then h may be rather larger than unity.[8b,21] Detailed experimental investigation of these reactions will be required before the importance of these points can be assessed.

With regard to the larger C_{14} hydrocarbons discussed in Parts II and III, the derived aza-heterocycles should behave in much the same way as the aza-azulenes, the polarisabilities in Table 1 showing that the differences between the different positions in the hydrocarbons are much larger than the effects of the nitrogen atom. It seems likely that this conclusion will apply to most of the $(4\gamma + 2)$ non-alternant hydrocarbons.

It has been supposed thus far that the change in Coulomb integral of the carbon atom is due to its replacement with a nitrogen atom. As discussed earlier, the inductive effect of substituents may also be represented in this way, but the values of the parameters h and k may require revision (see following paper).

Appendix

It is required to obtain eqn. (4) from eqn. (3).

We have

$$\pi_{t,p} = 4 \sum_{j=1}^{m} \sum_{k=m+1}^{n} \frac{c_{tj} \cdot c_{pj} \cdot c_{tk} \cdot c_{pk}}{(e_j - e_k)} \quad \ldots \ldots \quad \text{(as 3)}$$

Consider the term from a bonding cosine wave function molecular-orbital (ψ_j cos) with an antibonding cosine wave function orbital [ψ_k (cos)]. This is

$$\frac{\chi_j^2 \chi_k^2}{(e_j - e_k)} \cos\left(2tj\frac{\pi}{n} + \zeta_j\right) \cos\left(2pj\frac{\pi}{n} + \zeta_j\right) \cos\left(2tk\frac{\pi}{n} + \zeta_k\right) \cos\left(2pk\frac{\pi}{n} + \zeta_k\right)$$

[19] Dewar and Maitlas, *J.*, 1957, 944.
[20] R. D. Brown, *Trans. Faraday Soc.*, 1949, **45**, 296; 1950, **46**, 146.
[21] R. D. Brown, *Austral. J. Chem.*, 1956, **9**, 83.

and there is a second term from the same bonding orbital [ψ_j(cos)] with the antibonding sine wave function molecular-orbital [ψ_k(sin)]—

$$\frac{\chi_j^2\chi_k^2}{(e_j - e_k)} \cos\left(2tj\frac{\pi}{n} + \zeta_j\right) \cos\left(2pj\frac{\pi}{n} + \zeta_j\right) \sin\left(2tk\frac{\pi}{n} + \zeta_k\right) \sin\left(2pk\frac{\pi}{n} + \zeta_k\right)$$

From the sum of these two terms

$$\frac{\chi_j^2\chi_k^2}{(e_j - e_k)} \cos\left(2tj\frac{\pi}{n} + \zeta_j\right) \cos\left(2pj\frac{\pi}{n} + \zeta_j\right) \cos\left(2(t-p)k\frac{\pi}{n}\right) \quad . \quad . \quad (33)$$

there is another pair of terms from the bonding molecular-orbital having a sine wave function [ψ_j(sin)] with the same antibonding orbitals.

Summation of these two terms gives

$$\frac{\chi_j^2\chi_k^2}{(e_j - e_k)} \sin\left(2tj\frac{\pi}{n} + \zeta_j\right) \sin\left(2pj\frac{\pi}{n} + \zeta_j\right) \cos\left(2(t-p)k\frac{\pi}{n}\right) \quad . \quad . \quad (34)$$

Summing (33) and (34) and then summing over the totality of the molecular-orbitals, we obtain

$$\pi_{t,p} = 4 \sum_{j=0}^{\gamma} \sum_{k=\gamma+1}^{2\gamma+1} \frac{\chi_j^2\chi_k^2}{(e_j - e_k)} \cos 2(t-p)j\frac{\pi}{n} \cdot \cos 2(t-p)k\frac{\pi}{n} \quad . \quad . \quad (35)$$

The non-degenerate lowest bonding and highest antibonding molecular-orbitals are included in this summation as explained in Part III, Appendix 1.

When j and k are conjugate molecular-orbitals, *i.e.*, $k = [(2\gamma + 1) - j]$ and $e_k = -e_j$, the term within the summation sign is

$$\frac{\chi_j^4}{2e_j} \cos(t-p)\pi \cdot \cos^2\left\{2(t-p)j\frac{\pi}{n}\right\}$$

The total contribution to $\pi_{t,p}$ from such terms is

$$4 \sum_{j=0}^{\gamma} \frac{\chi_j^4}{2e_j} \cos(t-p)\pi \cdot \cos^2\left\{2(t-p)j\frac{\pi}{n}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (36)$$

The remaining terms are from the non-conjugate molecular-orbitals. Let the kth antibonding molecular-orbital be conjugate with the hth bonding molecular-orbital. Then $k = \{(2\gamma + 1) - h\}$, $e_k = -e_h$, and the term within the summation is

$$\frac{\chi_j^2\chi_h^2}{(e_j + e_h)} \cos(t-p)\pi \cdot \cos 2(t-p)j\frac{\pi}{n} \cdot \cos 2(t-p)h\frac{\pi}{n}$$

and there is another term from the bonding molecular-orbital (h) with the antibonding when $k = [(2\gamma + 1) - j]$, $e_k = -e_j$. This term is

$$\frac{\chi_j^2\chi_h^2}{(e_j + e_h)} \cos(t-p) \cdot \cos 2(t-p)j\frac{\pi}{n} \cdot \cos 2(t-p)h\frac{\pi}{n}$$

The sum of such terms is

$$8 \sum_{j=0}^{\gamma-1} \sum_{h=\gamma+1}^{\gamma} \frac{\chi_j^2\chi_h^2}{(e_j + e_h)} \cos(t-p)\pi \cdot \cos 2(t-p)j\frac{\pi}{n} \cdot \cos 2(t-p)h\frac{\pi}{n} \quad . \quad (37)$$

Combining (36) and (37), we have

$$\pi_{t,p} = 4\cos(t-p)\pi\left[\sum_{j=0}^{\gamma} \frac{\chi_j^2}{2e_j} \cos^2\left(2(t-p)j\frac{\pi}{n}\right) + 2\sum_{j=0}^{\gamma-1} \sum_{h=\gamma+1}^{\gamma} \frac{\chi_j^2\chi_h^2}{(e_j + e_h)} \cos 2(t-p)j\frac{\pi}{n} \cdot \cos 2(t-p)h\frac{\pi}{n}\right] \quad . \quad (4)$$

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770. *Structure and Properties of Mesomeric Systems. Part V.* The Effect of Substituents on the Chemical Reactivity of the* $(4\gamma + 2)$ *Non-alternant Hydrocarbons.*

By David Peters.

By making reasonable assumptions about the parameters, one can estimate the order of magnitude of the expected substituent effects in the $(4\gamma + 2)$ non-alternant hydrocarbons. The presence of one of the common substituents will probably have little or no effect on the orientation of ionic substitution in these hydrocarbons, a phenomenon which has already been discovered experimentally by Anderson and his co-workers.

In Parts I—III a new perturbation method was developed to predict the properties of some unknown $(4\gamma + 2)$ non-alternant hydrocarbons. Apart from its theoretical interest, such information is useful in synthesis, since it indicates the reaction conditions and isolation procedures which the products may survive. In Part IV these methods, extended to non-alternant aza-heterocycles, showed that the aza-azulenes should behave similarly to the parent hydrocarbon on substitution.

We now turn to substituents in $(4\gamma + 2)$ non-alternant hydrocarbons. This is of practical interest since it seems that substituents might "stabilise" (reduce the reactivity) of hydrocarbons difficult of synthesis.

Previous work on substituent action has been largely concerned with predicting their directive effects in benzene,[1,2,3,4] by solution of the secular equations for a range of parameter values and comparison of the results with experiment. The major effects of substituent action in benzene can be understood. We are now primarily concerned with the order of magnitude of the substituent effects, rather than with their directive action. As the former is a relatively gross effect (whether there is any directive effect) we may hope for success with a less accurate method of calculation. This makes perturbation methods[5,6,7] possible, which avoid the solving of large secular equations. Our method is based partly on the qualitatively successful resonance theory, ascribing substituent action to inductive and mesomeric effects.[1,4,8,9] The former is treated as for the introduction of the nitrogen atom, the Coulomb integral of the carbon atom to which the substituent is attached being supposed to differ from that of a normal one. The latter is represented by the action of an idealised substituent in which all the hetero-atoms have been replaced by carbon atoms. This procedure is unsatisfactory in that it will not reproduce all the phenomena of substituent action in benzene, but it does reproduce the two major phenomena of *ortho–para*-direction with activation and *meta*-direction with deactivation. For reasons given below, this method should be adequate for the non-alternant hydrocarbons in spite of its shortcomings for benzene. As azulenes containing substituents other than alkyl can now be prepared,[10] any information would be valuable in the formidable task of their orientation.

Method.—The inductive effect being treated in the same way as the introduction of a nitrogen atom, it remains to evaluate the mesomeric effect. Both the isolated-molecule

* Part IV, preceding paper.

[1] Wheland and Pauling, *J. Amer. Chem. Soc.*, 1935, **57**, 2086.
[2] Wheland, *ibid.*, 1942, **64**, 900.
[3] Dewar, *J.*, 1949, 463.
[4] Sandorfy, *Bull. Soc. chim. France*, 1949, **16**, 615.
[5] Jaffé, *J. Amer. Chem. Soc.*, 1955, **77**, 274.
[6] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 283.
[7] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341.
[8] *Idem, ibid.*, p. 3357.
[9] Peters, *J.*, 1957, 2654.
[10] Anderson, Nelson, and Tazuma, *J. Amer. Chem. Soc.*, 1953, **75**, 4980; Anderson, Cowles, Tazuma, and Nelson, *ibid.*, 1955, **77**, 6321; Anderson, Scotoni, Cowles, and Fritz, *J. Org. Chem.*, 1957, **22**, 1193.

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and the localisation approximations are used. Azulene is taken as a convenient model. Substituents are described as monatomic, diatomic, and triatomic when they contribute one (NR_2, OR), two (CO·R, CN), and three (CO_2R, NO_2*) atomic orbitals to the mesomeric system respectively. Overlap is neglected. For symbols, see the preceding paper.

Isolated-molecule Approximation.—We require the charge distribution in a cross-linked cyclic polyene carrying a group of one or more carbon atoms. Suppose atoms r and s of the cyclic polyene to be cross-linked and the attached group of carbon atoms, representing the substituent, to be joined by atom q to atom p of the cyclic polyene. Then the charge (q_t) on atom t is a function of β_{rs} and β_{pq} †

$$q_t' = q_t + (\partial q_t/\partial\beta_{rs})\delta\beta_{rs} + (\partial q_t/\partial\beta_{pq})\delta\beta_{pq} \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

together with higher terms which are neglected. The second term on the right-hand side of eqn. (1) represents the cross-linking of the cyclic polyene (Part III). The third term is a first-order perturbation expression for the charge differential produced by the idealised substituent. If the latter is represented by two carbon atoms (*i.e.*, CO·R, CN), then the perturbation vanishes, both the substituted and the unsubstituted cyclic polyene being alternant hydrocarbons. If the substituent is represented by three carbon atoms (CO_2R, NO_2), the charge developed in the ring is again zero, being confined to the terminal carbon atoms of the substituent. If the substituent is represented by a single carbon atom (*i.e.*, NR_2, OR), then there will be a charge developed in the ring, owing to the formation of a non-bonding molecular-orbital in the substituted cyclic polyene. This charge is immediately given by the well-known equation [11]

$$\sum_v c_{ov}\beta_{uv} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where the summation is over all atoms (v) adjacent to atom u and c_{ov} is the coefficient at atom v of the non-bonding molecular-orbital. We take the resonance integral of the bonds in the ring as β, the standard carbon–carbon bond resonance integral when overlap is neglected. There remains the resonance integral of the bond between the substituent and the ring (β_{pq}). It is commonly agreed that this should be substantially less than β. In the case of the halogens, experimental evidence is available from the nuclear quadrupole coupling data. Howe and Goldstein [12] find that β_{C-Cl} and β_{C-Br} must be taken as approximately 0·5β and 0·4β respectively in order to reproduce the ionisation potential and the charge transfer in vinyl chloride and bromide and in chloro- and bromo-benzene. These calculations, however, include overlap. Jaffé [13] finds that values in the range 0·06—0·89β are required for the halogens and alkoxyl and amino-groups in order to reproduce the Hammett σ constants for these substituents. Sandorfy [4] estimates these resonance integrals as 0·12—0·96β for the same substituents. The present author [9] has used values of 0·2—0·4β for the monatomic substituents in order to reproduce certain ultraviolet spectral data. Another [14] finds β_{CO} in phenols to be 0·27β. As we are seeking the order of magnitude of substituent effects rather than the details of their action, we do not differentiate between the monatomic substituents, but examine a single hypothetical substituent whose resonance integral with the ring is $\beta/3$—*i.e.*, whose mesomeric constant is $\frac{1}{3}$. The conclusions depend only on the fact that β_{pq} is substantially less than β, not on its exact value.

If this value is used for β_{pq}, eqn. (2) becomes, when atom u is atom p:

$$\sum_v' c_{ov}\beta + c_{oq}\beta/3 = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

* Attached to the ring by the centre, not by the terminal, atom.
† β_{pq} is the resonance integral of the bond between the substituent and the ring.

[11] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.
[12] Howe and Goldstein, *ibid.*, 1957, **27**, 831; 1957, **26**, 7; Goldstein, *ibid.*, 1956, **24**, 507.
[13] Jaffé, *J. Chem. Phys.*, 1952, **20**, 279.
[14] Lopex Vaquex, *Anales real soc. espan. Fis. Quim.*, 1955, **51**, 203.

The prime denotes that atom q is omitted from the summation. In this way, the mesomeric charges resulting from a monatomic substituent can be estimated for all positions of the $(4\gamma + 2)$ non-alternant hydrocarbons.

The Localisation Method.—Here we need the effect on the energy of the ground and the transition state of introducing extra carbon atoms into the mesomeric system. If the π-electron energy of the cyclic polyene is $E_{c.p.}$, the change in π-electron energy ($\delta E_{c.p.}$) on cross-linking atoms r and s and adding a new group of carbon atoms by atom q to atom p of the cyclic polyene is given by

$$\delta E_{c.p.} = (\partial E_{c.p.}/\partial\beta_{rs})\delta\beta_{rs} + (\partial E_{c.p.}/\partial\beta_{pq})\delta\beta_{pq} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

plus higher terms which are neglected. The change ($\delta E_{p.r.}$) in the π-electron energy of the polyene radical on cross-linking and addition of the idealised substituent is given by

$$\delta E_{p.r.} = (\partial E_{p.r.}/\partial\beta_{rs})\delta\beta_{rs} + (\partial E_{p.r.}/\partial\beta_{pq})\delta\beta_{pq} \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The localisation energy for free-radical attack ($\mathscr{E}_s$) in the cross-linked substituted cyclic polyene is then

$$\mathscr{E}_s = E_{c.p.} + \delta E_{c.p.} - E_{p.r.} - \delta E_{p.r.} = [E_{c.p.} + (\partial E_{c.p.}/\partial\beta_{rs})\delta\beta_{rs}] - [E_{p.r.} + (\partial E_{p.r.}/\partial\beta_{rs})\delta\beta_{rs}] + [(\partial E_{c.p.}/\partial\beta_{pq}) - (\partial E_{p.r.}/\partial\beta_{pq})]\delta\beta_{pq}$$

But from Part II (eqn. 1)

$$\mathscr{E}_a = [E_{c.p.} + (\partial E_{c.p.}/\partial\beta_{rs})\partial\beta_{rs}] - [E_{p.r.} + (\partial E_{p.r.}/\partial\beta_{rs})\delta\beta_{rs}] \quad . \quad . \quad . \quad . \quad (7)$$

where $\mathscr{E}_a$ is the atom localisation energy for free-radical substitution in the unsubstituted, cross-linked non-alternant hydrocarbon. Hence

$$\mathscr{E}_s = \mathscr{E}_a + [(\partial E_{c.p.}/\partial\beta_{pq}) - (\partial E_{p.r.}/\partial\beta_{pq})]\partial\beta_{pq} \quad . \quad . \quad . \quad . \quad . \quad (8)$$

Now the first-order perturbation term $\partial E_{c.p.}/\partial\beta_{pq}$ is zero. This is easily shown by writing the molecular-orbitals of the cyclic polyene as ψ_h and the molecular (atomic) orbitals of the substituent as ψ_s and then we have for the energies ($e_{c.p.}'$) of the perturbed molecular-orbitals of the cyclic polyene [7]

$$e_{c.p.}' = e_{c.p.} + \int\psi_h H'\psi_h d\tau \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

with a similar expression for the energies of the perturbed molecular-orbitals of the substituent. Expanding the molecular-orbitals into their constituent atomic orbitals (ϕ's), we have

$$\psi_h{}^a = \sum_n c_{an}\phi_h{}^n \qquad \psi_s{}^b = \sum_m c_{bm}\,\phi_s{}^m$$

and if it is assumed that the only non-vanishing term is $\int\phi_h{}^p H'\,\phi_s{}^q d\tau$ the first-order perturbation vanishes.

The second term in eqn. (8) is also a first-order perturbation expression, describing the interaction between the substituent and the residual molecule. If the substituent is represented by two carbon atoms (CO·R, CN), there is only accidental degeneracy between doubly-filled molecular-orbitals, and the situation is the same as in the cyclic polyene—the perturbation vanishes. For triatomic and monatomic substituents, there is degeneracy between the non-bonding molecular-orbital of the polyene radical and the zero-energy atomic (molecular) orbital of the idealised substituent. In this case [7]

$$e_{p.r.}{}^{0\prime} = e_{p.r.}{}^0 + c_{op} \cdot c_{oq} \cdot \beta_{pq} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where $e_{p.r.}^{0'}$ is the energy of the perturbed non-bonding molecular-orbital of the polyene radical and c_{op} and c_{oq} are the atomic orbital coefficients of the non-bonding molecular-orbitals of the polyene radical and the substituent respectively. For triatomic substituents, $c_{oq} = 0$ and the perturbation vanishes. For monatomic substituents, $c_{oq} = 1$, $\beta_{pq} = \beta/3$, and eqn. (10) becomes

$$e_{p.r.}^{0'} = e_{p.r.}^{0} + c_{op} \cdot \beta/3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Now if p is unstarred,[6,7] $c_{op} = 0$ and the perturbation vanishes. If p is starred, $c_{op} \neq 0$ and there is a first-order correction to the energy unless both non-bonding molecular-orbitals are doubly occupied. The common monatomic substituents all contribute two electrons to the mesomeric system, so that in nucleophilic substitution there is again no correction to the energy. In electrophilic substitution there is a decrease in the π-electron energy of the polyene radical which is given by

$$\delta E_{p.r.}/\delta\beta_{pq} = 2c_{op}/3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

or

$$\mathscr{E}_s^{+} = \mathscr{E}_a^{+} - 2c_{op}\beta/3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

Results.—In the Table the charge distribution and localisation energies of azulenes carrying a single monatomic substituent of inductive constant +1·0 and mesomeric constant $\frac{1}{3}$ are reported, calculated from eqns. (3) and (13) and data in the preceding paper. The charge distribution and localisation energies of azulene are taken from Parts II and III.

Distribution of charge $(1 - q_t)$ *and localisation energies (units of* β*) for electrophilic* $(\mathscr{E}_s^{+})$ *and nucleophilic* $(\mathscr{E}_s^{-})$ *processes for azulene and azulenes substituted with a single monatomic substituent at the position denoted by* **X**.

[Standard numbering: see preceding paper.]

Posn. (t)	1	2	3	4	5	6	7	8
Charge	−0·185	−0·056	−0·185	+0·163	+0·015	+0·144	+0·015	+0·163
$\mathscr{E}_s^{+}$	1·92	2·32	1·92	2·72	2·32	2·72	2·32	2·72
$\mathscr{E}_s^{-}$	2·72	2·32	2·72	1·92	2·32	1·92	2·32	1·92
Charge	**X**	−0·090	−0·141	+0·206	+0·052	+0·187	+0·052	+0·207
$\mathscr{E}_s^{+}$	**X**	2·22	2·06	2·86	2·22	2·86	2·22	2·86
$\mathscr{E}_s^{-}$	**X**	2·12	2·58	1·78	2·12	1·78	2·12	1·78
Charge	−0·219	**X**	−0·219	+0·200	+0·058	+0·181	+0·058	+0·200
$\mathscr{E}_s^{+}$	1·82	**X**	1·82	2·62	2·46	2·62	2·46	2·62
$\mathscr{E}_s^{-}$	2·52	**X**	2·52	1·72	2·18	1·72	2·18	1·72
Charge	−0·142	−0·019	−0·141	**X**	−0·019	+0·188	+0·052	+0·206
$\mathscr{E}_s^{+}$	2·06	2·22	2·06	**X**	2·22	2·86	2·22	2·86
$\mathscr{E}_s^{-}$	2·58	2·12	2·58	**X**	2·12	1·78	2·12	1·78
Charge	−0·095	−0·013	−0·148	+0·129	**X**	+0·110	+0·059	+0·200
$\mathscr{E}_s^{+}$	1·82	2·46	1·82	2·62	**X**	2·62	2·46	2·62
$\mathscr{E}_s^{-}$	2·52	2·18	2·52	1·72	**X**	1·72	2·18	1·72
Charge	−0·142	−0·019	−0·142	+0·207	−0·019	**X**	−0·019	+0·207
$\mathscr{E}_s^{+}$	2·06	2·22	2·06	2·86	2·22	**X**	2·22	2·86
$\mathscr{E}_s^{-}$	2·58	2·12	2·58	1·78	2·12	**X**	2·12	1·78

Discussion

The diatomic and triatomic substituents have, in this approximation, no mesomeric effect either on the charge distribution or on the localisation energies, so that their action is purely inductive. In Table 2 of the preceding paper the charge distribution and localisation energies of an azulene molecule which carries a single substituent whose inductive constant is +1·0 were reported. We now require the inductive constants of the diatomic and triatomic substituents. An attempt has been made [9] to estimate these from the σ constants of the Hammett $\rho\sigma$ equation, the results suggesting that the inductive

constants of all of the common substituents are in the range −0·1 to +1·0. Since a substituent whose inductive constant is at the upper limit of this range has only a minor effect on the charge distribution and localisation energies of azulene, we conclude that these substituents are unlikely to affect the orientation of ionic substitution in azulene.

The monatomic substituents are more complex. They have both inductive and mesomeric effects, usually in opposition. When one quite outweighs the other no difficulty arises, but when they are fairly evenly balanced—as with the halogens—it is not surprising that the crude Hückel method does not satisfactorily predict the small difference between two large quantities. Nevertheless, the figures in the Table show that, unless the method is completely misleading, these substituents also have only minor effects on the charge distribution and localisation energies of azulene. That is, the orientation of ionic substitution in a monosubstituted azulene will be the same as in the parent hydrocarbon and no directive effect analogous to that found in benzene is to be expected.

This conclusion agrees exactly with the known experimental facts. Anderson and his co-workers [10] prepared a number of mono- and di-substituted azulenes from azulene itself, introducing the substituents by substitutions which would be expected to be electrophilic. They state that the presence of one substituent does not affect the position of substitution for the second entering group, in agreement with the present conclusions. This is true for all of the substituents which they studied, regardless of their directive effect in benzene. Specifically, these workers found that 1-nitro-, 1-halogeno-, 1-acetamido-, 1-acetyl- and 1-methoxycarbonyl-azulene all undergo electrophilic substitutions such as nitration, acetylation, halogenation, and Friedel–Crafts benzylation in the 3-position. Furthermore, disubstitution often accompanies monosubstitution, showing that the presence of a substituent in the 1-position does not drastically deactivate the 3-position. Again, they have reported no instance of appreciable quantities of tri- or poly-substitution, showing that the two substituents in the 1- and the 3-position do not have any profound influence on the remaining positions. All this evidence is in line with the theory.

Returning to the predictions, we can say that the main conclusion will apply to all of the $(4\gamma + 2)$ non-alternant hydrocarbons having charge and localisation energy differentials comparable with those in azulene, a condition which is fulfilled by all those discussed in Parts II and III. This conclusion might be invalidated by a substituent whose inductive or mesomeric constant is much greater than the values used in this paper, but from experiment it seems unlikely that this will apply to common substituents.

The rate of substitution will be affected by the substituent, but it seems unlikely that the present crude method will suffice to predict this more subtle phenomenon with any accuracy. It is always possible that the mechanisms which operate in the benzenoid hydrocarbons will not always operate in non-alternant systems. If this is so, we may expect discrepancies between theory and experiment which will be useful in detecting these mechanistic changes.

The possibility that substituents could be used to " stabilise " non-alternant hydrocarbons which have proved difficult to prepare has clearly not been realised, the substituents having only minor effects on the chemical reactivity.

The author is indebted to Professor M. J. S. Dewar for advice.

Royal Holloway College, Englefield Green, Surrey. [*Received, April 29th*, 1958.]

771. *The Magnetic Properties of the Quinquevalent Complex Fluorides of Molybdenum, Tungsten, and Rhenium.*

By G. B. Hargreaves and R. D. Peacock.

The magnetic moments of the complex fluorides $MMoF_6$, MWF_6, and $MReF_6$ (where M is an alkali metal) have been measured over the temperature range 90—300° K.

Apart from the complex fluorides recently prepared in these laboratories, no compound of quinquevalent molybdenum, tungsten, and rhenium is known which contains discrete AX_6^- ions, although salts such as K_2MoOCl_5 (where the complex ion includes two different ligands) are well established. Recent interest in the magnetic behaviour of "*d*" block transition-metal ions has now led us to study this aspect of the properties of our compounds.

The complex fluorides have the low magnetic moments to be expected for transition-metal ions of the second or third Periods in these electronic configurations; the spin-only value for the salts $MMoF_6$ and MWF_6 ($d\varepsilon_1$ configuration) is $\mu = 1{\cdot}73$ B.M., and for the salts $MReF_6$ ($d\varepsilon_2$) is $\mu = 2{\cdot}83$ B.M. None of the moments follows the simple relation $\chi_A \propto 1/T$ (where T is the absolute temperature), but $MMoF_6$ and $MReF_6$ fit the Curie–Weiss relationship $\chi_A \propto 1/(T + \theta)$ but with rather large positive values of the Curie constant (Fig. 1 and Table 1). The plot $1/\chi_A$ against T for the tungsten salts does not give a straight line; hence there is undoubted antiferromagnetism with Néel points over the range 110—140° K.

Table 1.

	θ	$\mu_{calc.}$ (300°)		θ	$\mu_{calc.}$ (300°)		θ	$\mu_{calc.}$ (300°)		θ	$\mu_{calc.}$ (300°)
$NaMoF_6$	218	1·66	$RbMoF_6$	158	1·75	$NaReF_6$	100	1·57	$RbReF_6$	50	1·56
$KMoF_6$	66	1·51	$CsMoF_6$	224	1·66	$KReF_6$	58	2·05	$CsReF_6$	35	1·53

The simple idea of the magnetic behaviour of the "*d*" block elements which relates paramagnetism directly to the number of unpaired spins, whilst specially useful for the first transition series, is of less value when applied to the second and third rows. In particular, difficulties usually arise with d^2 and d^4 complexes of the heaviest transition elements. For second- and third-row transition elements spin–orbit coupling, which depends largely on nuclear charge and hence on atomic number, has also to be taken into account. In this discussion we follow the views of Earnshaw, Figgis, Lewis, and Nyholm,[1] who have applied Kotani's theory [2] to the magnetic behaviour of ruthenium and osmium compounds. The theory predicts magnetic moments of gaseous ions subjected to a cubic crystal field, so that when it is applied to solids departures from ideal behaviour may be expected. Fig. 2 shows the experimental change of μ_{eff} with T for the three series of salts, together with "ideal" plots of μ_{eff} expected for various values of the spin–orbit coupling constant A. It is relevant to note that for $d\varepsilon_1$ and $d\varepsilon_2$ configurations large changes in the spin–orbit coupling constant cause only small changes in the magnetic moment.

The graphs show that Kotani's theory cannot be applied directly to our compounds. In the case of the tungsten salts this is obviously because there is antiferromagnetism, and the nature of the other experimental curves suggests that in these cases also Néel points exist at temperatures below those at which our measurements were made. The antiferromagnetic interaction in these compounds is not likely to be of the normal type such as occurs in a perovskite lattice ABO_3 and is presumably similar to that observed by Owen *et al.*[3] in K_2IrCl_6. One point, however, which does emerge from the graphs in

[1] Earnshaw, Figgis, Lewis, and Nyholm, *Nature*, 1957, **179**, 1121.
[2] Kotani, *J. Phys. Soc. Japan*, 1949, **4**, 293.
[3] Griffiths, Owen, and Ward, *Proc. Roy. Soc.*, 1953, **219**, *A*, 526.

all three series of compounds is the different behaviour of the potassium salts from that of the rest. This is particularly noticeable in the rhenium series, and it is relevant to call attention to the structures of the salts.

The cubic sodium salts and the rhombohedral rubidium and cæsium salts undoubtedly

FIG. 1. *Plots of* $1/\chi_A$ *against absolute temperature.*

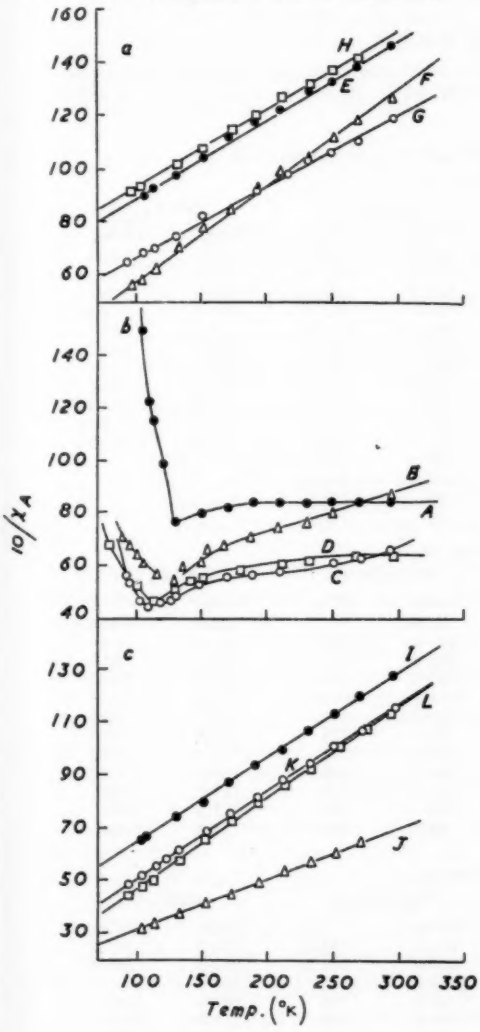
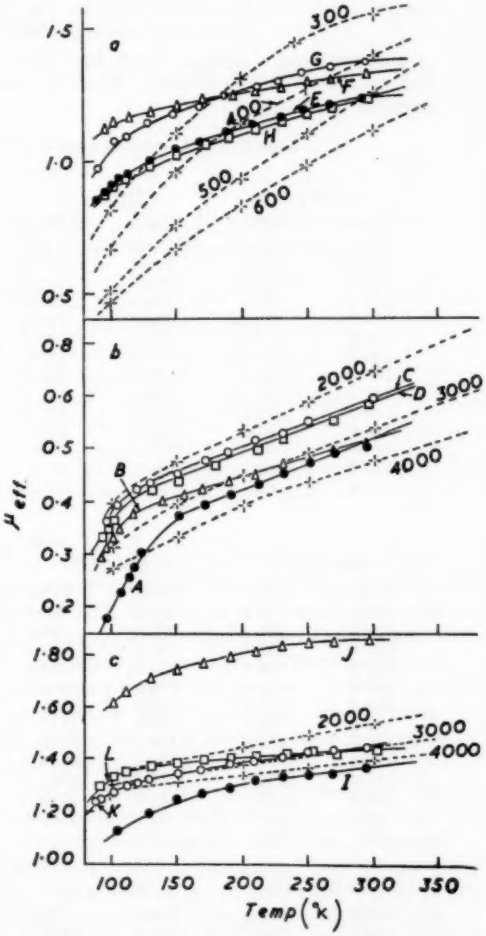


FIG. 2. *Plots of* μ_{eff} *against absolute temperature.*



a, $XMoF_6$ series; *b*, XWF_6 series; *c*, $XReF_6$ series. For individual compounds, see Table 2. Broken lines are theoretical curves calculated on the basis of values of *A* as marked thereon.

contain discrete AF_6^- (A = Mo, W, Re) octahedra with a single A–F distance.[5,6] But the potassium salts are tetragonally distorted, and a recent determination [4] of the structure

[4] Bode and Döhren, *Acta Cryst.*, 1958, **11**, 80.
[5] Hargreaves and Peacock, *J.*, 1957, 4212; Peacock, *J.*, 1957, 467.
[6] For the rhombohedral $KOsF_6$ structure see Hepworth, Jack, and Westland, *J. Inorg. Nucl. Chem.*, 1956, **2**, 79.

of $KNbF_6$, which is isostructural with our salts, has shown that in each NbF_6^- octahedron there are two shorter Nb–F distances and four longer ones. The difference between them is slight (~0·02 Å) and would not account for the differences in magnetic behaviour between the potassium salts and the rest if Kotani's theory alone were taken into account. However, a tetragonal distortion would also affect antiferromagnetic interaction, and could therefore have a disproportionately large effect on the magnetic moment.

Experimental

Quinquevalent Complex Fluorides.—The salts were prepared as described previously [5] and, except for KWF_6 (Found: W, 53·3. Calc.: W, 54·6), all analyses, carried out as before, gave the same figures.

Table 2. *Corrected molar susceptibilities (temperatures in* °K).

MWF_6 Series $d\varepsilon_1$

$NaWF_6$ (*A*)		KWF_6 (*B*)		$RbWF_6$ (*C*)		$CsWF_6$ (*D*)	
Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$
294·2	112·8	294·2	108·2	294·2	142·4	295·0	145·8
270·0	112·8	269·0	117·3	271·3	147·6	267·5	145·8
250·0	112·8	249·7	117·3	249·5	152·8	230·5	148·6
229·5	112·8	230·7	124·0	230·0	152·8	210·5	151·4
210·0	112·8	208·2	126·3	209·3	160·6	149·8	165·5
189·8	112·8	188·5	133·1	188·5	153·3	139·5	168·3
169·5	115·4	167·6	137·6	169·5	165·9	128·5	176·7
150·0	118·0	154·4	139·8	148·5	173·7	120·6	176·7
130·0	123·3	149·8	151·1	128·8	186·7	111·5	196·4
120·0	96·9	136·0	153·4	127·0	189·4	99·5	173·89
116·8	83·6	128·5	169·1	117	194·6	90·8	165·5
110·0	78·3	115·0	160·2	108	202·4		
105·0	65·1	104·0	151·1	102·8	194·6		
94·3	43·9	90	130·8	95	171·1		
				90	168·5		

$MMoF_6$ Series $d\varepsilon_1$

$NaMoF_6$ (*E*)		$KMoF_6$ (*F*)		$RbMoF_6$ (*G*)		$CsMoF_6$ (*H*)	
Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$
295·0	681·1	294·4	792·0	294·6	841·4	294·0	680·5
268·3	722·1	268·5	840·8	267·8	908·5	268·4	704·8
258·6	748·5	249·5	892·1	248·0	943·1	248·8	731·5
230·3	768·8	230·5	942·6	230·0	969·6	231·0	756·0
209·3	815·7	209·0	1008	214·3	1014	210·0	787·5
189·3	847·9	190·8	1074	189·8	1090	190·0	823·9
169·2	888·7	170·5	1171	169·0	1124	171·8	870·1
150·3	955·9	149·5	1279	149·0	1213	149·0	928·5
129·3	1017	130·5	1413	128·8	1340	130·0	977·2
112·5	1070	112·8	1581	112·0	1425	111·0	1062
105·4	1104	101·0	1710	103	1455	101·3	1069
93·3	1082	95·5	1746	90·0	1502	94·3	1089
88	1099						

$MReF_6$ Series $d\varepsilon_2$

$NaReF_6$ (*I*)		$KReF_6$ (*J*)		$RbReF_6$ (*K*)		$CsReF_6$ (*L*)	
Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$	Temp.	$10^6\chi_A$
294·2	792·7	295·4	1444	295·1	884·6	295·2	881·2
269·0	844·2	268·8	1585	269·5	952·3	269·5	940·4
250·0	894·3	250·0	1699	249·4	1015	250·8	1011
230·0	950·7	230·5	1818	229·8	1082	231·0	1088
210·0	1024	210·5	1943	209·4	1163	210·0	1177
190·3	1086	189·5	2106	190·3	1257	190·0	1283
169·5	1170	170·4	2279	169·2	1357	170·0	1408
149·5	1284	150·0	2507	150·8	1487	150·0	1567
129·3	1368	129·5	2783	129·3	1681	130·0	1787
104·0	1527	110·8	3087	120·0	1771	110·0	2054
102·5	1555	101·0	3232	112·0	1865	101·3	2166
				101·5	2000	90·0	2309
				90·8	2130		
				89·0	2135		

Magnetic Measurements.—These were made over the temperature range 90—300° K by the Gouy method. The apparatus was similar to that described by Figgis and Nyholm.[7] Since the salts are unstable in air, the powdered specimens were introduced into Pyrex magnetic tubes (whose diamagnetism had previously been determined) under vacuum. Results are shown in Table 2.

We are indebted to Dr. J. Lewis for valuable discussions, to Imperial Chemical Industries Limited, General Chemicals Division, Widnes, for the use of a fluorine cell, and to the Department of Scientific and Industrial Research for a maintenance grant (to G. B. H.).

IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, May 13th*, 1958.]

[7] Figgis and Nyholm, *J.*, in the press.

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772. *Pyrroles and Related Compounds. Part I. Syntheses of Some Unsymmetrical Pyrrolylmethylpyrroles (Pyrromethanes).*

By A. HAYES, G. W. KENNER, and N. R. WILLIAMS.

Unsymmetrical pyrrolylmethylpyrroles (pyrromethanes) (III) can be prepared from 5-bromomethylpyrroles (as I) and pyrrole-2-carboxylic acids (as II), either by brief heating in chloroform solution or by prolonged reaction between an alkali-metal salt of the acid and the pyridinium derivative of the halide (I). The analogous reaction with bicyclic carboxylic acids (III; R = H) is much less successful owing to formation of adducts with the probable structure (VII). The benzyl esters, from which the acids (II) are available, are conveniently prepared by alkoxide-catalysed transesterification of the ethyl esters.

RECENT biochemical studies [1] with isotopes have demonstrated that natural compounds of both the porphyrin and the chlorophyll series arise from porphobilinogen and, while the precise mechanism of this process is still being discussed, there is general agreement that the four pyrrole nuclei are linked by methylene groups before cyclisation and dehydrogenation. In contrast, the classical porphyrin syntheses [2] proceed through pyrromethenes, in which the link is a methine group. A notable exception is the method of Siedel and Winkler,[3] but this is not fully controllable and indeed it leads, somewhat unexpectedly, to type III porphyrins.[4] Hence further examination of controlled stepwise linking of pyrrole nuclei by methylene groups [5] seemed to us desirable.

This paper is mainly concerned with the first stage of such syntheses, namely, the linking of two pyrrole nuclei to afford a pyrromethane (systematically named pyrrolylmethylpyrroles). Reaction between an α-halogenomethylpyrrole and the Grignard derivative of another pyrrole is a method of achieving this condensation,[6] but we chose a slightly different plan permitting possible future extension to stepwise syntheses employing blocking groups. An obvious blocking group for a 2-position, which is to be substituted later by a cationoid reagent, is benzyloxycarbonyl since a 2-carboxyl group is very easily displaced by proton and by bromine.[7] 2-Benzyloxycarbonylpyrroles have

[1] CIBA Foundation, "Porphyrin Biosynthesis and Metabolism," Ed. Wolstenholme and Millar, Churchill, London, 1955.
[2] Fischer and Orth, "Chemie des Pyrrols," Akademische Verlag, Leipzig, 1937, Vol. II, Part 1, p. 160.
[3] Siedel and Winkler, *Annalen*, 1943, **554**, 162.
[4] Bullock, Johnson, Markham, and Shaw, *J.*, 1958, 1430.
[5] A related study has been reported by Corwin and Coolidge, *J. Amer. Chem. Soc.*, 1952, **74**, 5196.
[6] Fischer, Baumann, and Riedel, *Annalen*, 1929, **475**, 205.
[7] Fischer and Orth, "Die Chemie des Pyrrols," Akademische Verlag, Leipzig, 1934, Vol. I, pp. 85, 235.

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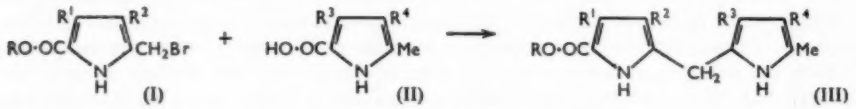
been prepared from benzyl acetoacetate by the Knorr method,[8] but we found it convenient to prepare them from the usual ethyl esters by alkoxide-catalysed transesterification; this reaction does not seem to have been used before, perhaps because the carbonyl group is inert and fairly drastic conditions are necessary, but the yields are good. Hydrogenolysis of the benzyl link is normal and this sequence provides clean preparations of, for instance, 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylic acid and, by decarboxylation with acid, cryptopyrrole.

For coupling with these carboxylic acids, the esters derived from oxy-acids and hydroxymethylpyrroles were expected to be suitable and there seemed to be an easy route through the acetoxymethyl compounds, prepared from the methylpyrroles and lead tetra-acetate.[3] However, we were unable to prepare ethyl 4-ethyl-5-hydroxymethyl-3-methylpyrrole-2-carboxylate by alkaline hydrolysis of its acetyl derivative; only gums were obtained from most of the varied experiments, but some 25% of the crystalline methoxymethyl derivative was isolated after treatment with potassium hydroxide in aqueous methanol. Incidentally, it was shown by acetyl analysis and infrared spectroscopy that the material described by Siedel and Winkler [3] as the hydroxymethylpyrrole is actually its acetyl derivative, as indeed would be expected from its formation by action of lead tetra-acetate on ethyl 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylate. Moreover, the 2-benzyloxymethylpyrrole proved quite inert during attempted hydrogenolysis, and no crystalline product could be isolated from reactions between either silver diphenyl phosphate or silver toluene-*p*-sulphonate with ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate. Accordingly this approach was abandoned in favour of more direct use of α-bromomethylpyrroles and, in fact, two good methods of condensing them with pyrrole-2-carboxylic acids were discovered; several examples of each method are given in the Experimental section. Incidentally, bromination of α-methylpyrroles in cold dilute ethereal solution gave more reliable preparations of these intermediates than the usual method with warm acetic acid.

The simpler and usually preferable method is to boil a solution of the reagents, (I) and (II), in dry chloroform for 10 minutes, whereupon hydrogen bromide and carbon dioxide are evolved and the pyrromethane is obtained in about 75% yield; the reaction is favoured



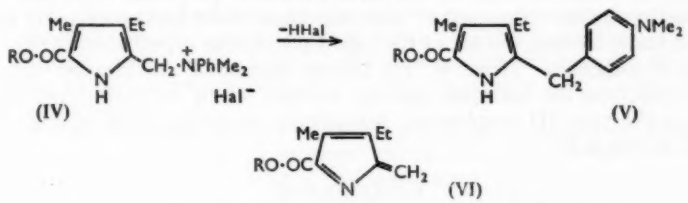
by a low dielectric constant, being faster in benzene and slower in nitromethane. As pyrrole-2-carboxylic acids lose carbon dioxide very easily, particularly under acidic conditions, it seemed possible that decarboxylation preceded condensation. But reaction between 3-ethyl-2 : 4-dimethylpyrrole (cryptopyrrole) and a bromomethylpyrrole (I; $R = CH_2Ph$, $R^1 = Me$, $R^2 = Et$) gave less than 6% of the pyrromethane under conditions which produced 80% from the carboxylic acid. Evidently the carboxylic acid is the true reagent, and indeed it is natural that it should be more reactive in cationoid substitution than the product of its decarboxylation, which is itself a cationoid substitution, and likewise salts of the carboxylic acid should be even more easily substituted. However, while lithium 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylate did react moderately well with a bromomethylpyrrole (I; $R = R^2 = Et$, $R^1 = Me$), the reaction was slow and it may actually have gone through gradual liberation of some hydrogen bromide and hence the free acid.

On the other hand carboxylate salts are employed in the second method together with α-pyridiniummethylpyrrole bromides, prepared by quaternisation of α-bromomethylpyrroles. This reaction, in contrast to the other, requires a very polar medium and even

[8] MacDonald, *J.*, 1952, 4176.

aqueous mixtures containing 65% dimethylformamide or 50% acetone or 90% methyl cyanide were unsatisfactory. Good results were obtained with pure formamide but aqueous methanol is the most generally useful solvent; if the reagents are mixed in aqueous solution, there is immediate precipitation of an oil and therefore the best practice is to use the minimum proportion of methanol which prevents this precipitation. In order to reduce side-reactions, a moderate temperature is advisable despite the slowness of the reaction. It was expected that the rate would increase when a weaker base than pyridine was used for quaternisation and decrease when a stronger base was used; in fact the reaction proceeded less satisfactorily with 2-chloropyridine, 2 : 4-dimethylthiazole, triethylamine, or 4-methylmorpholine. When cryptopyrrole was substituted for the corresponding carboxylate salt, the yield fell by more than half. While this effect is less marked than in the first method, it seems that here again carbon dioxide is expelled during cationoid substitution.

An attempted modification of the second, quaternary salt method was unsuccessful because of an interesting rearrangement. Our idea was to employ the 2-methylphenylaminomethyl group as a comparatively inert substituent which could be activated by quaternisation at a suitable stage in a polypyrrole synthesis. This was frustrated by the very ready conversion by bases of the quaternary salts (IV) into the *p*-dimethylaminophenylmethylpyrroles (V). Oxidation with dichromate or permanganate produced the expected reddish-purple (Ehrlich) colour from these rearranged materials. Their structures were shown in infrared spectra, dissociation constants, and, in the instance of the benzyl ester (V; R = CH_2Ph), alternative synthesis from *p*-dimethylaminobenzoic acid and benzyl 4-ethyl-5-methoxy-3-methylmethylpyrrole-2-carboxylate. The analogous reactions took place with derivatives of diethylaniline. Presumably the base removes a proton from the cyclic nitrogen atom and thus decomposes the quaternary salt to the highly reactive intermediate (VI). Bearing this hypothesis in mind, we have sought alkaline catalysis of the reaction between α-bromomethylpyrroles and pyrrole-2-carboxylate salts, but without noteworthy result.

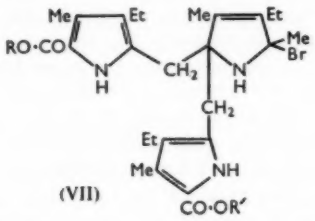


One serious limitation of both synthetical methods is that they apparently fail completely when α-methoxymethyl- or α-acetoxymethyl-pyrroles are used instead of the α-methylpyrroles (II). Coupling with 3-2′-carboxyethyl-4 : 5-dimethylpyrrole-2-carboxylic acid (II; $R^3 = CH_2{\cdot}CH_2{\cdot}CO_2H$, R^4 = Me) and its derivatives was also unexpectedly difficult. Both methods were tried unsuccessfully with the diacid, its salts, and its monomethyl ester. The nitrile (II; $R^3 = CH_2{\cdot}CH_2{\cdot}CN$, R^4 = Me) seemed to be a hopeful alternative, but the intermediate amide, benzyl 3-2′-carbamoylethyl-4 : 5-dimethylpyrrole-2-carboxylate, was obtained in only 25% yield from the diester; the 2-carboxylic acid derived from it also failed to react with benzyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate (I; R = CH_2Ph, R^1 = Me, R^2 = Et). During the preparation of this series of pyrroles, the β-methyl group was introduced by Treibs and Zinsmeister's method [9] with the convenient modification that the Mannich base was prepared directly from the β-carboxylic acid.

Another limitation is that side-reactions become important, or overwhelming, when the process is extended to reaction between a pyrromethane acid (III; R = H) and an

[9] Treibs and Zinsmeister, *Chem. Ber.*, 1957, **90**, 87.

α-bromomethylpyrrole (I). Coupling by the first method of the pyrromethane acid (III; R = H, $R^1 = R^3 = Me$, $R^2 = R^4 = Et$) with both the ethyl and the benzyl ester



(VII)

(I; R = Et or CH_2Ph, $R^1 = Me$, $R^2 = Et$) led to crystalline substances with the composition of simple adducts. Brief treatment of these adducts with boiling ethanolamine gave small amounts of the pyrromethane esters (III; R = Et or CH_2Ph, $R^1 = R^3 = Me$, $R^2 = R^4 = Et$). Further an adduct was still obtained when a pyrromethane ester was used instead of the free acid. Provisionally we assign to these adducts the structure (VII), or the ionic equivalent; their reaction with alcoholic silver nitrate is rapid but scarcely decisive.

The second, quaternary salt method was more successful. A minute yield of the " tripyrrane " (pyrrolylmethylpyrrolylmethylpyrrole) was obtained from the lithium salt (III; R = Li, $R^1 = R^3 = Me$, $R^2 = R^4 = Et$) and the pyridinium derivative of the bromomethylpyrrole (I; $R = CH_2Ph$, $R^1 = Me$, $R^2 = Et$), but another lithium salt (III; R = Li, $R^1 = R^3 = Me$, $R^2 = Et$, $R^4 = CO_2Et$) yielded 23% of the crystalline " tripyrrane." Very likely the reactions with quaternary salts and with bromomethylpyrroles have the same side path and this is made less accessible by an appropriately placed ethoxycarbonyl substituent.

It should be remarked that the self-condensation of porphobilinogen may follow, at any rate partly, similar " side-paths " and that these could lead to type III porphyrins, which are actually formed, instead of the type I porphyrins expected from the " normal " elimination of ammonia. However, the factors controlling the relative importance of the various reactions are uncertain and the schemes which we have drawn do not lead inevitably to the type III porphyrins; accordingly we refrain from adding yet another speculation in this field.

Experimental

Benzyl 4-Ethyl-3 : 5-dimethylpyrrole-2-carboxylate.—A mixture of ethyl 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylate [10] (100 g.), sodium (2 g.), and benzyl alcohol (250 c.c.) was kept at 100° with exclusion of moisture during 1 hr., then ethanol was distilled away at 12 mm. This operation was repeated periodically until, after 4 hr. in all, the solution was evaporated on a water-bath at 1 mm. The residue was taken up in ether (500 c.c.), which was washed with water and then kept overnight in the refrigerator. The *benzyl ester* which crystallised was combined with the second crop and recrystallised from light petroleum (b. p. 80—100°) in colourless needles (115 g., 87%), m. p. 104—105° (Found: C, 75·0; H, 7·2; N, 5·7. $C_{16}H_{19}O_2N$ requires C, 74·7; H, 7·4; N, 5·4%).

Benzyl 3 : 5-Dimethylpyrrole-2-carboxylate.—Sodium (0·5 g.) and ethyl 3 : 5-dimethylpyrrole-2-carboxylate [11] (21 g.) in benzyl alcohol (150 c.c.) were manipulated as in the preceding experiment. Recrystallisation of the *benzyl ester* as above afforded 17 g. (60%) having m. p. 102—104° (Found: C, 73·3; H, 6·7; N, 6·3. $C_{14}H_{15}O_2N$ requires C, 73·3; H, 6·6; N, 6·1%).

2-Benzyl 4-Ethyl 3 : 5-Dimethylpyrrole-2 : 4-dicarboxylate.—The usual Knorr synthesis was carried out with benzyl acetoacetate (40 g.) in glacial acetic acid (60 c.c.) and sodium nitrite (15 g.) in water (20 c.c.), ethyl acetoacetate (27 g.) in glacial acetic acid (110 c.c.), and zinc

[10] Signaigo and Adkins, *J. Amer. Chem. Soc.*, 1936, **58**, 709.
[11] Chu and Chu, *J. Org. Chem.*, 1954, **19**, 266.

dust (40 g.). Two recrystallisations from ethanol of the crude *diester* (44 g.) afforded 23 g. (40%), m. p. 122—123° (Found: C, 68·1; H, 6·5; N, 4·9. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4; N, 4·65%).

Ethyl 4-*Diethylaminomethyl*-3-(2-*ethoxycarbonylethyl*)-5-*methylpyrrole*-2-*carboxylate*.—5-Ethoxycarbonyl-4-(2-ethoxycarbonylethyl)-2-methylpyrrole-3-carboxylic acid was prepared from its benzyl ester according to MacDonald's directions;[3] in large-scale working it was preferable to dissolve the product of hydrogenolysis in boiling ethanol (3 l. for 200 g.), filter off the catalyst, and allow crystallisation to occur instead of forming the sodium salt. A mixture of the acid (149 g.), diethylamine (102 c.c.), 40% aqueous formaldehyde (59 c.c.), and ethanol (400 c.c.) was boiled under reflux during 5 hr., before being filtered and poured into water (4·5 l.). A little unchanged acid (3·5 g.) was collected when the pH had been brought down to 2 with dilute hydrochloric acid, and the filtrate was then made alkaline with aqueous ammonia. The *Mannich base* (149 g., 90%) having m. p. 57—58°, which crystallised out of the cooled solution, was sufficiently pure for hydrogenolysis, but recrystallisation from aqueous methanol furnished material with m. p. 66—67° (Found: C, 63·0; H, 8·9; N, 7·9%; equiv., 328. $C_{18}H_{30}O_4N_2$ requires C, 63·9; H, 8·9; N, 8·3%; equiv., 338).

Ethyl 3-(2-*Ethoxycarbonylethyl*)-4 : 5-*dimethylpyrrole*-2-*carboxylate*.—The foregoing Mannich base (79·3 g.) and Raney nickel (20 c.c.) in ethanol (500 c.c.) were stirred with hydrogen (100 atm.) at 150° during 10½ hr. The filtered solution was combined with another batch and concentrated under reduced pressure to 300 c.c. The solution was boiled and brought to the point of crystallisation by addition of water. A portion of the *diethyl ester*, m. p. 88—90° (94 g., 80%), recrystallised from aqueous ethanol in chunky crystals, m. p. 91° (Found: C, 63·0; H, 7·9; N, 5·4. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·9; N, 5·2%).

Benzyl 3-(2-*Benzyloxycarbonylethyl*)-4 : 5-*dimethylpyrrole*-2-*carboxylate*.—The foregoing diethyl ester (80 g.), sodium (4 g.), and benzyl alcohol (400 c.c.) were heated at 13 mm. on a boiling-water bath during 2½ hr. The residue from evaporation of the benzyl alcohol at 100°/2 mm. was dissolved in benzene (500 c.c.) and washed with water (4 × 75 c.c.). Dilution of the benzene solution, after it had been dried and concentrated to 200 c.c., with light petroleum furnished the *dibenzyl ester* (55 g., 47%), m. p. 130° unchanged by recrystallisation from methanol (in plates) (Found: C, 73·3; H, 6·8; N, 3·7. $C_{24}H_{25}O_4N$ requires C, 73·6; H, 6·4; N, 3·6%).

Acidification with acetic acid of the aqueous wash-liquor precipitated benzyl 3-(2-carboxyethyl)-4 : 5-dimethylpyrrole-2-carboxylate (38 g., 42%), m. p. 165—167° (Found: equiv., 307. Calc. for $C_{17}H_{19}O_4N$: equiv., 301). Presumably its sodium salt was formed while the benzene solution of the dibenzyl ester was washed, and this could have been avoided by previous addition of carbon dioxide.

Benzyl 3-(2-*Methoxycarbonylethyl*)-4 : 5-*dimethylpyrrole*-2-*carboxylate*.—(*a*) Sodium (0·1 g.) was added to a solution of the foregoing dibenzyl ester (5 g.) in methanol (50 c.c.). Solid carbon dioxide was added to the solution after it had been boiled during 20 min. and it was then concentrated to 15 c.c. and diluted with water (5 c.c.). The *methyl benzyl ester* (3·5 g., 87%) crystallised in needles, m. p. 93—95° raised to 95° by recrystallisation from methanol (Found: C, 68·3; H, 6·7; N, 4·5. $C_{18}H_{21}O_4N$ requires C, 68·5; H, 6·7; N, 4·4%).

(*b*) A solution of the foregoing monobenzyl ester (37 g.) in methanol (150 c.c.) was boiled during 1 hr. while being saturated with dry hydrogen chloride. Evaporation to 50 c.c., crystallisation, and recrystallisation from aqueous methanol (charcoal) furnished 26 g. (68%) of mixed ester, m. p. 94—95°.

Benzyl 3-(2-*Carbamoylethyl*)-4 : 5-*dimethylpyrrole*-2-*carboxylate*.—The foregoing methyl benzyl ester (2 g.) and methanol (30 c.c.) saturated with ammonia were kept in a sealed tube at 160° during 48 hr. Evaporation followed by recrystallisation from chloroform and then methanol afforded 0·5 g. (25%) of the *amide*, m. p. 210—212° raised to 214—215° by two further crystallisations from chloroform (Found: C, 67·9; H, 7·0; N, 9·0. $C_{17}H_{20}O_3N_2$ requires C, 68·0; H, 6·7; N, 9·3%). The infrared spectrum (Nujol mull) contained, as expected, major bands at 1672, 1660 cm.$^{-1}$ and a smaller one at 1625 cm.$^{-1}$.

Ethyl 4-(2-*Benzyloxycarbonylethyl*)-3 : 5-*dimethylpyrrole*-2-*carboxylate*.—Sodium (0·1 g.) was added to a solution of ethyl 4-(2-ethoxycarbonylethyl)-3 : 5-dimethylpyrrole-2-carboxylate (5 g.) in benzyl alcohol (50 c.c.). After the solution had been heated on a boiling-water bath at 13 mm. during 4 hr., it was evaporated at 2 mm. The residual *benzyl ethyl ester* was washed in ether with water before being crystallised from methanol; it had m. p. 68—70° (4·6 g., 75%)

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and recrystallised from light petroleum (b. p. 80—100°) in needles, m. p. 69—71° (Found: C, 68·9; H, 7·5; N, 4·1. $C_{19}H_{23}O_4N$ requires C, 69·3; H, 7·0; N, 4·25%).

Ethyl 4-(2-*Methoxycarbonylethyl*)-3 : 5-*dimethylpyrrole*-2-*carboxylate*.—This preparation from the foregoing benzyl ethyl ester followed preparation (*a*) above of benzyl 3-(2-methoxycarbonylethyl)-4 : 5-dimethylpyrrole-2-carboxylate. The *ethyl methyl ester*, m. p. 100—102°, was obtained in 85% yield and, recrystallised from aqueous methanol, had m. p. 102° (Found: C, 61·7; H, 7·5; N, 5·7. $C_{13}H_{19}O_4N$ requires C, 61·6; H, 7·6; N, 5·5%).

Benzyl 4-(2-*Benzyloxycarbonylethyl*)-3 : 5-*dimethylpyrrole*-2-*carboxylate*.—The foregoing ethyl methyl ester (1·2 g.), sodium (0·2 g.), and benzyl alcohol (30 c.c.) were heated on a boiling-water bath at 13 mm. during 7 hr. The *dibenzyl ester*, m. p. 86—88° (1·2 g., 84%), was isolated in the usual way and recrystallised from methanol in needles, m. p. 87—88° (Found: C, 73·8; H, 6·6; N, 3·7. $C_{24}H_{25}O_4N$ requires C, 73·6; H, 6·4; N, 3·6%).

Benzyl 4-(2-*Methoxycarbonylethyl*)-3 : 5-*dimethylpyrrole*-2-*carboxylate*.—This *benzyl methyl ester* was prepared from the foregoing dibenzyl ester in the same way as the isomeric ester; the yield of material with m. p. 97—99° was 87% and, recrystallised from methanol, had m. p. 99—100° (Found: N, 4·4%).

Ethyl 5-*Acetoxymethyl*-4-*ethyl*-3-*methylpyrrole*-2-*carboxylate*.—Treatment of ethyl 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylate with lead tetra-acetate in glacial acetic acid at room temperature according to Siedel and Winkler's method [3] produced the 2-acetoxymethylpyrrole (43%), which was recrystallised from light petroleum (b. p. 80—100°) and sublimed at 110°/0·01 mm., then having m. p. 127—128° (Found: C, 61·6; H, 7·3; N, 5·8; Ac, 17·7. Calc. for $C_{13}H_{19}O_4N$: C, 61·6; H, 7·6; N, 5·5; Ac, 17·0%). A saturated solution of this substance in carbon tetrachloride had peaks of infrared absorption at 1745, 1721, 1701, 1678 cm.$^{-1}$, whereas a solution of the precursory 2-methylpyrrole had peaks at 1715, 1669 cm.$^{-1}$.

Hydrolysis of this 2-acetoxymethylpyrrole with potassium hydroxide in methanol or ethanol gave the 2-methoxymethyl- and 2-ethoxymethyl-pyrrole, which are described below. Hydrolysis with potassium hydroxide in cold 50% aqueous acetone or with sodium hydrogen carbonate in boiling 50% aqueous acetone yielded a brown gum together with small amounts of a colourless crystalline *substance*, m. p. 102—104°, possibly the symmetrical ether (Found: C, 64·8; H, 7·3; N, 6·4. $C_{22}H_{32}O_5N_2$ requires C, 65·3; H, 8·0; N, 6·9%).

Benzyl 5-*Acetoxymethyl*-3-*methylpyrrole*-2-*carboxylate*.—This *compound* was obtained from benzyl 3 : 5-dimethylpyrrole-2-carboxylate in only 8% yield by the procedure described [3] for reaction between ethyl 3 : 5-dimethylpyrrole-2-carboxylate and lead tetra-acetate. Crystallisation from light petroleum (b. p. 80—100°) and sublimation at 100°/10^{-2} mm. furnished colourless crystals, m. p. 121° (Found: C, 66·9; H, 5·8; N, 5·2. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 6·0; N, 4·9%).

Ethyl 4-*Ethyl*-5-*methoxymethyl*-3-*methylpyrrole*-2-*carboxylate*.—The corresponding 2-bromomethylpyrrole, prepared as described below, was dissolved in hot methanol, which was promptly diluted with water till the appearance of turbidity. The methyl ether, which separated from the cooled solution in quantitative yield, was recrystallised from light petroleum (b. p. 80—100°) and sublimed at 60°/0·001 mm.; it had m. p. 75—77° (Found: C, 63·9; H, 8·4; N, 6·4. Calc. for $C_{12}H_{19}O_3N$: C, 64·0; H, 8·5; N, 6·2%). Fischer and Adler [12] give m. p. 73°.

Ethyl 5-*Ethoxymethyl*-4-*ethyl*-3-*methylpyrrole*-2-*carboxylate*.—This ethyl ether was obtained from the 2-acetoxymethylpyrrole and potassium hydroxide in cold ethanol, or better sodium ethoxide in boiling ethanol; it had m. p. 59—60° (Found: C, 65·0; H, 8·7; N, 5·9. Calc. for $C_{13}H_{21}O_3N$: C, 65·2; H, 8·8; N, 5·85%). Fischer and Adler [12] give m. p. 54° and Bullock *et al.*[4] give m. p. 56—58°.

Ethyl 5-*Benzyloxymethyl*-4-*ethyl*-3-*methylpyrrole*-2-*carboxylate*.—Ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate (4·0 g.) was dissolved in a solution of sodium (0·35 g.) in benzyl alcohol (25 c.c.). After removal of the sodium bromide, most of the benzyl alcohol was evaporated at 2 mm. Recrystallisation of the crystalline residue (2·45 g., 56%) from light petroleum (b. p. 80—100°) furnished the colourless *benzyl ether*, m. p. 85—86° (Found: C, 71·4; H, 7·2; N, 4·6. $C_{18}H_{23}O_3N$ requires C, 71·7; H, 7·7; N, 4·65%). This was recovered unchanged after attempted hydrogenolysis at room temperature and pressure in ether catalysed by platinic oxide, palladium black, or palladised charcoal, and in ethanol catalysed by Raney nickel.

Benzyl 4-*Ethyl*-5-*methoxymethyl*-3-*methylpyrrole*-2-*carboxylate*.—This *ether* was prepared like the ethyl ester in 90% yield with m. p. 85—86°, raised to 86—87° by recrystallisation from light

[12] Fischer and Adler, *Z. physiol. Chem.*, 1931, **197**, 266.

petroleum (b. p. 80—100°) (Found: C, 71·1; H, 7·3; N, 5·2. $C_{17}H_{21}O_3N$ requires C, 71·0; H, 7·4; N, 4·9%).

Benzyl 5-Benzyloxymethyl-4-ethyl-4-methylpyrrole-2-carboxylate.—This *benzyl ether* was made in 39% yield in the same way as the corresponding ethyl ester, and it had m. p. 99—100° after distillation at 120°/0·01 mm. (Found: C, 75·7; H, 6·9. $C_{32}H_{35}O_3N$ requires C, 76·0; H, 6·9%).

α-Bromomethylpyrroles (I).—A solution of bromine (2·8 c.c., one mol.) in dry ether (500 c.c.) was added rapidly to a vigorously stirred solution of ethyl 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylate (10 g.) in dry ether (500 c.c.). After 1 hr. the colour had faded to pale yellow, and the solution was then concentrated in a vacuum to about 200 c.c. The mass of crystals and liquor was left overnight in a refrigerator before being filtered; the colourless needles (11·7—13·2 g., 83—93%) of ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate, which easily became red in air, had m. p. 128—130° (Fischer and Ernst [13] record m. p. 128—132°). The analogous benzyl ester, m. p. 137—138°, was prepared in yields of 74—92%. Smaller-scale preparations were made of ethyl 5-bromomethyl-4-(2-ethoxycarbonylethyl)-3-methyl- (77%), m. p. 126—128°, ethyl 4-(2-benzyloxycarbonylethyl)-5-bromomethyl-3-methyl- (56%), m. p. 121—123°, benzyl 5-bromomethyl-4-(2-methoxycarbonylethyl)-3-methyl- (80%), m. p. 116—118°, and benzyl 5-bromomethyl-3-(2-methoxycarbonylethyl)-4-methyl-pyrrole-2-carboxylate (84%), m. p. 137—139°, which were intermediates in the preparations of pyrromethanes 6, 7, 8, and 9 respectively.

As the starting material was insufficiently soluble in ether, diethyl 5-bromoethyl-3-methylpyrrole-2 : 4-dicarboxylate was prepared according to ref. 14.

Pyrrole-2-carboxylic Acids (II).—(a) *From benzyl esters.* A solution of the benzyl pyrrole-2-carboxylate (3 g.) in methanol (150 c.c.) was shaken at room temperature and pressure with hydrogen and catalyst [15] (0·3 g.) containing 10% palladium–charcoal which had been washed with 10% nitric acid. Uptake of hydrogen was complete in about 4 hr. and the product was obtained as a cream-coloured powder by evaporation of the filtered solution under reduced pressure (nitrogen) at 40°; it was normally used immediately.

Alternatively, commercial ether containing two drops of triethylamine was substituted for the methanol. Then the course of hydrogenation could not be observed accurately, but it was complete in 2 hr. and the pure product was easily obtained by evaporation at 15°. In this way *4-ethyl-3 : 5-dimethylpyrrole-2-carboxylic acid*, previously described [16] as exceptionally unstable, was obtained with m. p. 102—103° (92%) and, recrystallised from 70% ethanol, had m. p. 104° with decarboxylation (Found: C, 65·0; H, 7·7; N, 8·7. $C_9H_{13}O_2N$ requires C, 64·65; H, 7·8; N, 8·4%). When a lithium salt was required, the ethereal solution was neutralised with N-methanolic lithium methoxide; in some cases the salt crystallised and in others the risk of decarboxylation during evaporation was reduced.

(b) *From ethyl esters.* When the sodium salt was required, the usual hydrolysis with sodium hydroxide (1·3 mols.) in boiling aqueous methanol (finally 50%) during 7 hr. was convenient; at first only two-thirds of the aqueous sodium hydroxide solution were added to the methanolic solution of the ester. An 80% yield was assumed and the solution was neutralised (phenolphthalein) with acetic acid before direct reaction with a pyridinium salt. The exceptionally stable 4-ethyl 2-hydrogen 3 : 5-dimethylpyrrole-2 : 4-dicarboxylate was prepared in this way [m. p. 203° (decomp.) after precipitation with dilute hydrochloric acid] in preference to hydrogenolysis of the benzyl ester, which gave colourless needles with m. p. 205—207° (decomp.).

Pyrrolylmethylpyrroles (*Dipyrromethanes*) (III).—*Method A.* Apart from variations in scale all the tabulated preparations were made as follows. The α-bromomethylpyrrole (I) (0·01 mol.) was added to a solution of the carboxylic acid (II) prepared directly from 1·05 mols. of the benzyl ester in chloroform (100 c.c. distilled from phosphoric oxide). Air was then displaced by nitrogen from the flask and reflux condenser, which was capped with a Bunsen valve. Immediately after the solution had been boiled during 10 min., it was evaporated under reduced pressure (nitrogen bubbler) to a light brown syrup, which was taken up in methanol (30 c.c.), treated with the appropriate small amount of water, and left in a refrigerator. The crystals, which were formed overnight in the tabulated yield, were fawn-coloured, and their m. p. was about 2° below that of the analytical specimen.

[13] Fischer and Ernst, *Annalen*, 1926, **447**, 139.
[14] Fischer and Stangler, *Annalen*, 1927, **459**, 53.
[15] Mozingo, *Org. Synth.*, 1946, **26**, 77.
[16] Fischer and Walach, *Ber.*, 1925, **58**, 2818.

Preparations of pyrromethane **2** in different solvents (boiling for stated time) gave the following yields: chloroform (30 min.) 41%; chloroform *not* dried with phosphoric oxide (10 min.) 56%; benzene (1 min.) 47%; nitromethane (30 min.) 50%, (60 min.) 68%, (90 min.) 38%; nitromethane *not* dried with phosphoric oxide (30 min.), 29% of impure material; methyl cyanide (30 min.), 50% of impure material. A preparation under the standard conditions from 3-ethyl-2 : 4-dimethylpyrrole, instead of the carboxylic acid, gave 5·5%.

Variations in the preparation of pyrromethane **1** gave the following yields: benzene (1 min.) 50%, (30 min.) 38%, (120 min.) 15%; methanol (30 min.) 31%. Under the standard conditions 44% was obtained from ethyl 5-chloromethyl-4-ethyl-3-methylpyrrole-2-carboxylate (from the 2-methylpyrrole and sulphuryl chloride [17] in 7% yield). The α-bromomethylpyrrole and the lithium salt of the carboxylic acid dissolved together in boiling benzene and then lithium bromide began to separate; after 2 hr. the solution contained a 43% yield of pyrromethane **1** and these seemed to be the optimum conditions. Lower yields were obtained from methanolic reaction mixtures.

Method B. Ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate (12 g.) dissolved exothermically in dry pyridine (15 c.c.), and this solution was used directly in reactions. Crystallisation of the quaternary salt from the cooled solution was assisted by addition of dioxan; after recrystallisation from dioxan, *1-(5-ethoxycarbonyl-3-ethyl-4-methyl-2-pyrrolylmethyl)pyridinium bromide* had m. p. 151—154° (Found: C, 54·1; H, 6·0; N, 7·7. $C_{16}H_{21}O_2N_2Br$ requires C, 54·4; H, 5·9; N, 7·9%). Slightly more pyridine (20 c.c.) was used to dissolve the corresponding benzyl ester (14·8 g.). The pyridine solution of either quaternary salt was diluted with 200 c.c. of the aqueous-alcoholic solvent (see below) and then mixed with a solution of either the sodium or the lithium salt (one mol.) in the same solvent (100 c.c.). The flask was flushed with nitrogen and capped with a Bunsen valve. The product usually crystallised during the reaction period; it was collected from the cooled mixture and washed with 50% and then 100% methanol. The tabulated preparations were carried out with the following solvents and times of heating: no. 1 in 25% methanol for 24 hr. at 40°; no. 2 in 50% methanol for 21 hr. at 40°; no. 3 in 50% methanol for 24 hr. at 40°; no. 4 in 50% ethanol for 9 hr. under reflux; no. 5 in 50% ethanol for 20 hr. under reflux.

Numerous trial preparations of pyrromethanes **1** and **2** were made on 1/10 scale. In addition to the points mentioned in the Introduction, it was found that reaction at room temperature yielded more than 50% after one week, that the excess of pyridine was valuable, and that reaction in 3 : 1 formamide–methanol gave a very impure product.

TABLE 1. *Pyrrolylmethylpyrroles (pyrromethanes)* (III).

No.	R	R¹	R²	R³	R⁴	Method	Yield (%)	M. p.[a]	Formula[d]
1	Et	Me	Et	Me	Et	A	68	141—142°[b]	$C_{19}H_{28}O_2N_2$
						B	75		
2	CH_2Ph	Me	Et	Me	Et	A	80	123—125	$C_{24}H_{30}O_2N_2$
						B	74		
3	Et	Me	Et	Me	H	B	69	129[c]	$C_{17}H_{24}O_2N_2$
4	Et	Me	Et	Me	CO_2Et	B	82	133—134	$C_{20}H_{28}O_4N_2$
5	CH_2Ph	Me	Et	Me	CO_2Et	B	78	164—165	$C_{25}H_{30}O_4N_2$
6	Et	Me	$CH_2{\cdot}CH_2{\cdot}CO_2Et$	Me	Et	A	83	116—118	$C_{23}H_{32}O_4N_2$
7	Et	Me	$CH_2{\cdot}CH_2{\cdot}CO_2{\cdot}CH_2Ph$	Me	Et	A	68	123—125	$C_{27}H_{34}O_4N_2$
8	CH_2Ph	Me	$CH_2{\cdot}CH_2{\cdot}CO_2Me$	Me	Et	A	40	125	$C_{26}H_{32}O_4N_2$
9	CH_2Ph	$CH_2{\cdot}CH_2{\cdot}CO_2Me$	Me	Me	Et	A	79	133—135	$C_{26}H_{32}O_4N_2$

[a] Recryst. from light petroleum (b. p. 80—100°) or ethanol. [b] Undepressed by a sample prepared according to ref. 6. [c] Fischer *et al.*[6] give m. p. 129°. [d] Analysis of the products for carbon, hydrogen, and nitrogen gave the following results (%) (figures required by the formulæ being in parentheses): no. 2, 76·3 (76·2), 7·8 (8·0), 7·4 (7·4); no. 4, 66·4 (66·6), 7·6 (7·8), 8·0 (7·8); no. 5, 71·3 (71·1), 7·1 (7·2), 6·7 (6·6); no. 6, 67·8 (68·0), 8·4 (8·3), 7·2 (7·2); no. 7, 72·1 (72·0), 7·9 (7·6), 6·3 (6·2); no. 8, 71·5 (71·5), 7·4 (7·4), —; no. 9, 71·3 (71·5), 7·4 (7·4), 6·4 (6·4).

Alkyl 5-Alkylanilinomethyl-4-ethyl-3-methylpyrrole-2-carboxylates.—A solution of either *N*-methylaniline or *N*-ethylaniline (2·0 mmol.) in dry ether (10 c.c.) was mixed with one of either ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate or the analogous benzyl ester (2·0 mmol.) in dry ether (30 c.c.). The hydrobromide of the product was rapidly

[17] Fischer, Sturm, and Friedrich, *Annalen*, 1928, **461**, 244.

precipitated and the solution was concentrated to 15 c.c. and washed with 1% ammonia solution. The brown gum obtained from the ether, after it had been washed with water and dried (K_2CO_3), was crystallised from ethanol. The *alkylanilinomethylpyrroles* (Table 2), obtained in good yield, were insoluble in cold ethanol but dissolved on the addition of dilute mineral acid.

TABLE 2. *Alkyl 5-Alkylanilinomethyl-4-ethyl-3-methylpyrrole-2-carboxylates.*

					Found (%)			Reqd. (%)		
Cpd.	*N*-Alkyl	Ester	M. p.	Formula	C	H	N	C	H	N
A	Me	Et	89—90°	$C_{18}H_{24}O_2N_2$	72·1	8·0	9·1	72·0	8·0	9·3
B	Me	CH_2Ph	91—92	$C_{23}H_{26}O_2N_2$	76·5	7·5	7·6	76·2	7·2	7·7
C	Et	Et	91—92	$C_{19}H_{26}O_2N_2$	72·9	8·5	8·6	72·6	8·3	8·9
D	Et	CH_2Ph	69—70	$C_{24}H_{28}O_2N_2$	76·8	7·8	7·2	76·6	7·5	7·4

Alkyl 5-Dialkylaminophenylmethyl-4-ethyl-3-methylpyrrole-2-carboxylates.—(*a*) A mixture of ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate or the benzyl ester (2 mmol.) and *NN*-dimethyl- or *NN*-diethyl-aniline (3 c.c.) was warmed on a water-bath for 2 min., then poured into 3N-hydrochloric acid (50 c.c.). The oily salt precipitated was taken up in 70% ethanol (10 c.c.) and decomposed with 10% ammonia solution (5 c.c.). The precipitated *dialkylaminophenylmethylpyrrole* (Table 3) was recrystallised from ethanol.

(*b*) The *NN*-dialkyl-*N*-(2-pyrrolylmethyl)anilinium salts were prepared from methyl or ethyl iodide and the compounds described in Table 2, or from the dialkylaniline and α-bromomethylpyrrole in cold ether. They formed colourless crystals, soluble in aqueous ethanol, and easily decomposed to gums. On being kept in 50% methanol with lithium 4-ethyl-3 : 5-dimethylpyrrole-2-carboxylate, they were converted into substances identified by mixed m. p. with those prepared by method (*a*).

(*c*) Concentrated hydrochloric acid (2 drops) was added to a solution of benzyl 4-ethyl-5-methoxymethyl-3-methylpyrrole-2-carboxylate (0·1 g.) and *p*-dimethylaminobenzoic acid (0·2 g.) in methanol (5 c.c.). After the solution had been boiled during 5 min., it was poured into dilute hydrochloric acid. Addition of ammonia solution to a solution of the precipitated solid in aqueous ethanol precipitated compound B′ (0·1 g.), m. p. 133—135° undepressed by material prepared by method (*a*). A similar yield was obtained from dimethylaniline (0·3 c.c.).

Physical Properties of Compounds Described in Tables 2 and 3.—Dissociation constants were determined by titration in 80% ethanol at 25°. Compound A′, pK_a' 4·2, like *NN*-dimethyl-*p*-toluidine pK_a' (4·2); compound C′, pK_a' 5·6; compound D′ pK_a' 5·3. The "unrearranged bases" were notably weaker and the following values are less accurate; compound A, pK_a' 1·8; compound C, pK_a' 3·8; compound D, pK_a' 3·6.

TABLE 3. *Ethyl or benzyl 5-dialkylaminophenylmethyl-4-ethyl-3-methylpyrrole-2-carboxylates.*

					Found (%)			Reqd. (%)		
Cpd.	*N*-Dialkyl	Ester	M. p.	Formula	C	H	N	C	H	N
A′	Me	Et	114—115°	$C_{18}H_{26}O_2N_2$	72·8	8·3	8·6	72·6	8·3	8·9
B′	Me	CH_2Ph	133—134	$C_{24}H_{28}O_2N_2$	76·4	7·3	7·7	76·6	7·5	7·4
C′	Et	Et	86—87	$C_{21}H_{30}O_2N_2$	73·8	8·5	7·9	73·6	8·8	8·2
D′	Et	CH_2Ph	87—88	$C_{26}H_{32}O_2N_2$	77·1	8·0	6·7	77·2	8·0	6·9

The infrared absorption of solutions in CCl_4 of all eight compounds was examined with Perkin-Elmer 21 machines (NaCl prism). The spectra in the "rearranged" series (Table 3) had a sharp peak (N–H) between 3430 and 3420 cm.$^{-1}$, a broad one (bonded N–H) at 3295—3285 cm.$^{-1}$, and a double peak at 1707—1705 and 1687—1680 cm.$^{-1}$. Spectra taken at various dilutions of compound A′ showed the diminution of the bonded N–H band expected for intermolecular hydrogen-bonding, but there was little change in the relative intensities of the twin peaks. The bonded N–H band was almost absent from the spectra in the "unarranged" series (Table 2), which were otherwise similar with peaks at 3430—3428, 1708—1707, 1690—1685 cm.$^{-1}$.

The absorption of the four ethyl esters was also examined for CS_2 solutions. In agreement with the assigned structures, the spectra of A and C have peaks at 746—742 and 687—683 cm.$^{-1}$

(monosubstituted benzene), while those of A′ and C′ have peaks at 809—802 cm.$^{-1}$ (*para*-disubstituted benzene). A peak at 767—766 cm.$^{-1}$ is common to all four spectra, and it is probably connected with the heterocyclic ring. Maxima: with A at 3420, 3285, 3020, 2955, 1706, 1684, 1316, 1240, 1182, 1110, 1068, 1060, 1030, 995, 962, 927, 766, 687 cm.$^{-1}$; with A′ at 3425, 3290, 2960, 1702, 1680, 1347, 1318, 1242, 1190, 1160, 1150, 1108, 1068, 1062, 1024, 975, 947, 809, 766 cm.$^{-1}$; with C at 3428, 2960, 1705, 1685, 1318, 1233, 1182, 1106, 1068, 1060, 1035, 962, 762, 742, 683 cm.$^{-1}$; with C′ at 3425, 3290, 2960, 1700, 1678, 1315, 1260, 1238, 1190, 1146, 1103, 1092, 1068, 1060, 1018, 972, 802, 763 cm.$^{-1}$.

Adducts (VII) *from α-Bromomethylpyrroles and Pyrromethanes.*—(*a*) A solution of pyrromethane **2** (1·9 g.) in methanol (180 c.c.) was shaken with 10% palladised charcoal (0·3 g.) and hydrogen until absorption of gas ceased (3 hr.). The acid left after filtration and evaporation was dissolved in dry chloroform (170 c.c.), mixed with ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate (1·23 g.), and boiled in an atmosphere of nitrogen during 10 min. The dark tar left after evaporation of the chloroform yielded 0·70 g. of crystals, m. p. 140—142, when its solution in ethyl acetate was chilled. Two recrystallisations from ethyl acetate–light petroleum furnished pink clusters of the *adduct* (VII; R = H, R′ = Et), m. p. 172—174° (Found: C, 60·0; H, 7·0; N, 7·1. $C_{38}H_{46}O_4N_3Br$ requires C, 59·8; H, 7·2; N, 7·5%). A solution of this adduct (0·3 g.) in 2-aminoethanol (2 c.c.) was boiled during 2 min. (slight effervescence), and was then poured into water (75 c.c.). Recrystallisation of the precipitate from aqueous methanol yielded pyrromethane **1** (0·05 g.), m. p. and mixed m. p. 140—142°.

(*b*) In the same manner benzyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate (0·75 g.) and pyrromethane **2** (0·70 g.) yielded the *adduct* (VII; R = H, R′ = CH_2Ph) (0·8 g.) as fawn rosettes, m. p. 137—139° raised to 143—145° by recrystallisation from chloroform–light petroleum (Found: C, 63·6; H, 6·9; N, 6·65. $C_{33}H_{42}O_4N_3Br$ requires C, 63·5; H, 6·8; N, 6·7%). Treatment of this adduct with 2-aminoethanol as described in (*a*) produced pyrromethane **2**, m. p. and mixed m. p. 123—125°.

(*c*) A solution of pyrromethane **2** (1·9 g.) and ethyl 5-bromomethyl-4-ethyl-3-methylpyrrole-2-carboxylate (1·03 g.) in dry chloroform (100 c.c.) was boiled during 10 min. in nitrogen. Evaporation and crystallisation from ethyl acetate furnished the *adduct* (VII; R = Et, R′ = CH_2Ph) (0·2 g.), m. p. 161—162° raised to 163—165° by recrystallisation from ethyl acetate–light petroleum (b. p. 80—100°) in brown plates (Found: C, 63·5; H, 7·1; N, 6·25. $C_{35}H_{46}O_4N_3Br$ requires C, 64·4; H, 7·1; N, 6·4%).

Benzyl 4-Ethyl-5-[5′-(4″-ethyl-3″ : 5″-dimethyl-2″-pyrrolylmethyl)-4′-ethyl-3′-methyl-2′-pyrrolylmethyl]-3-methylpyrrole-2-carboxylate.—Hydrogenolysis of pyrromethane **2** in ether by the method described above for the pyrrole series, followed by cautious recrystallisation from ethanol, yielded 83% of the carboxylic acid, m. p. 141—142° (decomp.) (lit.,[6] m. p. 145°). The lithium salt was obtained in the usual way in almost quantitative yield and was coupled with 1-(5-benzyloxycarbonyl-3-ethyl-4-methyl-2-pyrrolylmethyl)pyridinium bromide at 40° in 50% methanol. Within a few hours a dark brown oil has separated, and this also occurred under all the other conditions tried. When this oil was kept at 0° with a little ethanol the pale brown *product* separated in 1—5% yield; it had m. p. 120—122° after recrystallisation from ethanol (Found: C, 76·4; H, 8·0; N, 7·7. $C_{32}H_{41}O_2N_3$ requires C, 76·9; H, 8·3; N, 8·4%).

Ethyl 4-Ethyl-5-[5′-(4″-ethoxycarbonyl-3 : 5-dimethyl-2″-pyrrolylmethyl)-4′-ethyl-3′-methyl-2′-pyrrolylmethyl]-3-methylpyrrole-2-carboxylate.—Hydrogenolysis of pyrromethane **5** in ether was troublesome on account of its small solubility. While boiling during 1 hr., 150 c.c. of ether dissolved 1·35 g. of pyrromethane **5**, and the rapidly cooled solution was used immediately. The acid, m. p. 155—157° (decomp.), was obtained in quantitative yield. Its lithium salt, prepared directly from the ethereal solution, was coupled in 50% methanol at 40° with 1-(5-ethoxycarbonyl-3-ethyl-4-methyl-2-pyrrolylmethyl)pyridinium bromide. This mixture yielded a yellow gum together with the pale brown *product* (23%), m. p. 151—153° (from ethanol) (Found: C, 69·8; H, 8·1; N, 8·9. $C_{26}H_{38}O_4N_2$ requires C, 69·8; H, 8·2; N, 8·7%).

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773. *The Reaction between Aromatic Compounds and Derivatives of Tertiary Acids. Part XI.* Friedel–Crafts Reactions with Optically Active Acid Chlorides.*

By William Bleazard and Eugene Rothstein.

Friedel–Crafts reactions of optically active phenyl-*p*-tolyl- and *p*-chlorodiphenyl-acetyl chloride with anisole afford inactive ketones, but the active ketones are obtained from methylphenyl-*p*-tolyl- and ethylmethyl-*n*-propyl-acetyl chloride. An active ketone has not been isolated from (+)-*tert.*-butylmethyl*neo*pentylacetyl chloride because this substance expels carbon monoxide even in the above favourable conditions but with phenol in the presence of aluminium chloride the optically active phenyl ester is isolated. Inactive products are obtained from all the above acid chlorides if the reaction is carried out so as to eliminate carbon monoxide, *i.e.*, in benzene solution.

The synthesis of optically active ketones by means of the Friedel–Crafts reaction has not hitherto been described. The only record of an attempted preparation of this kind is that of McKenzie and Widdows [1] who condensed (+)-phenyl-*p*-tolylacetyl chloride with benzene but failed to obtain the expected ketone; instead, a mixture largely consisting of diphenyl- and triphenyl-methane and of triphenylmethanol was isolated.[2] The synthesis of a ketone from the inactive acid chloride by substituting anisole for benzene was carried out by Rothstein and Saville.[3] They showed that, in benzene solution, the non-production of a ketone resulted from the preferential elimination of carbon monoxide by the acid derivative. McKenzie and Widdows originally believed that they had isolated the inactive ketone but, although this was erroneous, they made the correct inference that the presence of an α-hydrogen atom leads to racemization and in analogy contrasted the optical stability of atrolactic acid towards alkali with that of its lower homologue mandelic acid which racemizes easily. This optical instability of secondary diarylacetyl chlorides has now been confirmed in the cases of (+)-phenyl-*p*-tolylacetyl chloride and (+)-α-*p*-chlorophenyl-α-phenylacetyl chloride, both of which yield inactive ketones when condensed with anisole. Racemization is of course due to the potential keto-enol system and is only indirectly connected with the Friedel–Crafts reaction itself because whereas *p*-tolyl is an activating group, *p*-chlorophenyl greatly decelerates both ketone formation and elimination of carbon monoxide.[4] A less effective enolizing agent might perhaps distinguish between the two acid halides since in somewhat analogous circumstances Conant and Carlson [5] observed a difference between, for example, (+)-αβ-diphenylpropionyl chloride which reacts with phenylzinc chloride to yield (+)-αβ-diphenylpropiophenone and (+)-phenyl-*p*-tolylacetyl chloride which as in the Friedel–Crafts reaction affords the inactive ketone only.

McKenzie and Widdows had, by implication, expected that a tertiary optically active acid should condense without recemization though they had not envisaged that under some conditions the loss of carbon monoxide might vitiate the experiment. This has been prevented by using anisole as the aromatic component and the first established case of an asymmetric synthesis using the Friedel–Crafts reaction is now recorded, (−)-*p*-methoxyphenyl 1-phenyl-1-*p*-tolylpropyl ketone having been prepared from (−)-α-phenyl-α-*p*-tolylpropionyl chloride:

$$CMePhTol{\cdot}COCl + MeOPh \longrightarrow CMePhTol{\cdot}CO{\cdot}C_6H_4{\cdot}OMe$$

* Part X, *J.*, 1958, 581.

[1] McKenzie and Widdows, *J.*, 1915, **107**, 702.
[2] McKenzie, Roger, and McKay, *J.*, 1932, 2597; Koelsch, *J. Amer. Chem. Soc.*, 1932, **54**, 4048.
[3] Rothstein and Saville, *J.*, 1949, 1961.
[4] Grundy, Hsü, and Rothstein, unpublished work.
[5] Conant and Carlson, *J. Amer. Chem. Soc.*, 1932, **54**, 4048.

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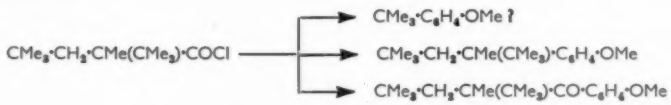
In Part V [3] and in subsequent papers of this series the hypothesis was adopted that elimination of carbon monoxide proceeds through an intermediate complex the decomposition of which is not affected by any subsequent reaction. The zero-order with respect to the aromatic component indicates, for instance, that transition complexes such as $ArH \ldots CR_3{\cdot}CO^+\}AlCl_4^-$ are not intermediates. The formation of optically active ketones, on the other hand, makes it evident that only after separation of the carbonyl group will the asymmetric carbon atom become planar. The separation should occur provided that structural considerations do not preserve a tetrahedral structure since the known properties of a tertiary carbonium ion do not suggest that this configuration would be stabilised solely by the electrostatic attraction of the aluminium tetrachloride anion. It follows that in general an optically active tertiary acid chloride should yield an inactive hydrocarbon CRR'R''Ar, but in selecting an example which would illustrate this point care had to be taken that the carbonium ion $^+CRR'R''$ did not undergo rearrangement or disintegration. For this reason the phenyl-*p*-tolylpropionyl chloride used above was unsuitable because, as was shown by Rothstein and Saville,[6] the lower homologue, *i.e.*, αα-diphenylpropionyl chloride with benzene affords a mixture of diphenylethane and a polymer of triphenylmethane. It has not yet been possible to identify the products from (−)-phenyl-*p*-tolylpropionyl chloride, but an inactive mixture apparently containing diphenyl- and diphenyl-*p*-tolyl-ethane is obtained. In the aliphatic series, disruption of the carbonium ion may also occur, especially if highly ramified chains are present. The reaction between benzene and (+)-2 : 2 : 3 : 5 : 5-pentamethylhexane-3-carbonyl chloride (*tert.*-butylmethyl*neo*pentylacetyl chloride) afforded at least five fractions, whose boiling points covered a range of 80° at 9 mm. and which mostly contained oxygen. Fragmentation when anisole was used was less evident. The product was also inactive, the main portion appearing to contain *tert.*-butylanisole and the remainder a mixture of 3-methoxyphenyl-2 : 2 : 3 : 5 : 5-pentamethylhexane, a trace of the corresponding ketone, 1-*tert.*-butyl-1 : 3 : 3-trimethylbutyl methoxyphenyl ketone with possibly other fragments and rearrangement entities:



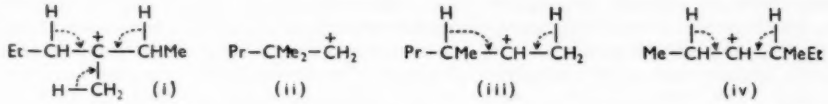
For both the above acid chlorides it was apparent that disruption of the molecule was consequent on the appearance of the carbonium ion; the retention of optical activity when (−)-phenyl-*p*-tolylpropionyl chloride was converted into the ketone demonstrated that the catalyst itself had no direct effect on the carbon skeleton. Furthermore, though it was not possible to obtain a ketone from (+)-*tert.*-butylmethyl*neo*pentylacetyl chloride, the reaction of the latter with phenol in the presence of aluminium chloride afforded an excellent yield of the (+)-phenyl ester, there being no racemization as far as could be judged.*

There remained the need to ascertain whether the carbonium ion formed by elimination of carbon monoxide was sufficiently free to assume a planar configuration. The simplest optically active aliphatic acid chloride which should yield a non-rearranging carbonium ion is 3-methylhexane-3-carbonyl chloride (ethylmethyl-*n*-propylacetyl chloride). Examination of the carbonium ion (i) derived from it shows that hyperconjugation

* It has been suggested that, in solution, aluminium chloride reacts with phenol to form phenoxyaluminium dichloride which is the esterifying agent. Even if this is the case this would not completely deactivate the compound as a catalyst in the Friedel–Crafts reaction since phenoxyaluminium dichloride can react with acetyl chloride, affording excellent yields of the hydroxyacetophenones (cf. Norris and Sturgis, *J. Amer. Chem. Soc.*, 1939, **61**, 1413).

[6] Rothstein and Saville, *J.*, 1949, 1946.

(indicated by dotted arrows) stabilises it in comparison with other rearranged structures (ii—iv):



The experimental results showed that the (+)-acid chloride which yielded a (+)-ketone when condensed with anisole, probably afforded inactive 3-methyl-3-phenylhexane with benzene. The Table below summarizes the optical properties of the acids and ketones derived from them.

Optical activity of acids and their related ketones.

	$RR'R''C\cdot CO_2H$		Alkaloid used for resolution	Optical activity of: acid	ketone
R	R′	R″	—	$[\alpha]_D^{18}$ solvent	$[\alpha]_D^{18}$ solvent
H	Ph	*p*-Tol	Cinchonidine	+14·4° $CHCl_3$	Inactive
H	Ph	*p*-C_6H_4Cl	Cinchonidine	+15·3° EtOH	Inactive
Me	Ph	*p*-Tol	Quinine	−11·0° $CHCl_3$	−12·1° $CHCl_3$
Me	CMe_3	$CH_2\cdot CMe_3$	Cinchonine	+23·8° EtOH	+24·5° * EtOH
Me	Et	Pr^n	Brucine	+19·7° EtOH	+14·5° $CHCl_3$

* Phenyl ester of original acid.

Experimental

Optical rotations were measured with $l = \frac{1}{2}$ or 1, and $c = 2 - 10$.

Preparation of Materials.—(+)-*Phenyl*-p-*tolylacetic acid.* The *cinchonidine salt* [1] (Found: C, 78·2; H, 7·0; N, 5·2. $C_{34}H_{36}O_3N_2$ requires C, 78·4; H, 7·0; N, 5·4%) yielded (+)-phenyl-*p*-tolylacetic acid, m. p. 82°, $[\alpha]_D^{18}$ 14·4° (in chloroform) (Found: C, 79·4; H, 6·1. Calc. for $C_{15}H_{14}O_2$: C, 79·6; H, 6·2%). McKenzie and Widdows found m. p. 83—84°, $[\alpha]_D$ +14·6° (in acetone). The *acid chloride* (formed by use of thionyl chloride, 75%) had b. p. 136°/0·1 mm. (Found: C, 73·7; H, 5·0; Cl, 14·7. $C_{15}H_{13}OCl$ requires C, 73·6; H, 5·3; Cl, 14·5%). It was optically active but precise measurements were not made.

(+)-α-p-*Chlorophenyl-α-phenylacetic acid.* Cinchonidine (98 g.) was gradually added to a boiling ethanolic solution (1·5 l.) of inactive α-*p*-chlorophenyl-α-phenylacetic acid [4] (82 g.). The liquid was boiled under reflux for 30 min. and sufficient water was added to produce cloudiness. The cooled solution deposited *cinchonidine* α-p-*chlorophenyl-α-phenylacetate*, m. p. 160° (74 g.) (Found: C, 73·7; H, 6·3; N, 5·1; Cl, 6·7. $C_{33}H_{33}O_3N_2Cl$ requires C, 73·3; H, 6·1; N, 5·2; Cl, 6·7%). Eight recrystallisations of the cinchonidine salt from 60% aqueous acetone afforded the optically pure salt (12 g.). This was decomposed by dilute sulphuric acid, and the precipitated (+)-α-*p*-chlorophenyl-α-phenylacetic acid recrystallised from dilute acetic acid. It had m. p. 112° and $[\alpha]_D^{18}$ 15·3° (in ethanol).

α-*Phenyl*-α-p-*tolylpropionic acid.* (i) Anhydrous stannic chloride (60 g.) was gradually added to a stirred boiling solution of atrolactic acid [7] (12 g.) in toluene (250 c.c.) and the whole was heated until no more hydrogen chloride was evolved. The liquid was mixed with water, and the toluene layer extracted with dilute sodium carbonate solution. The alkaline layer yielded a yellow oil when acidified, which on drying and admixture with benzene afforded a crystalline acid, m. p. 185—190°. This was shaken with concentrated hydrochloric acid. Crystallisation from dilute ethanol afforded isotropic acid (1-phenyltetralin-1 : 4-dicarboxylic acid), m. p. 238°, formed by the condensation of two molecules of atrolactic acid (Found: C, 72·9; H, 5·8. Calc. for $C_{18}H_{16}O_4$: C, 73·0; H, 5·4%).

A second method of preparation using aluminium chloride as the condensing agent [8] yielded only the starting material.

(ii) The synthesis finally adopted was that of Ramart and Amagat [9] who however did not record any yields. Benzyl phenyl-*p*-tolylacetate, b. p. 205—206°/0·05 mm. (130 g., 80%), was

[7] *Org. Synth.*, 1953, **33**, 7.
[8] Wegmann and Dahn, *Helv. Chim. Acta*, 1946, **29**, 426.
[9] Ramart and Amagat, *Ann. Chim.* (*France*), 1927, **8**, 276.

obtained by boiling the acid chloride (135 g.) with benzyl alcohol (500 c.c.) under reflux for 12 hr. Dibenzyl ether, b. p. 110°/0·2 mm. (80 g.), was also isolated. The benzyl ester (126 g.) was then boiled for 2 hr. under reflux with a suspension of sodamide (from 9 g. of sodium) in benzene (500 c.c.) and then for a further 12 hr. with methyl iodide (60 g.). The product, b. p. 195—200°/0·05 mm. (81 g., 60%), was hydrolysed with ethanolic potassium hydroxide, affording a yellow syrupy acid (52 g., 93%). The quinine salt was recrystallised eleven times from 50% aqueous acetone and on decomposition afforded (−)-α-*phenyl*-α-p-*tolylpropionic acid*, m. p. 96°, $[\alpha]_D^{18}$ −11·0° (7%) (Found: C, 80·2; H, 6·7. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%).

(+)-2 : 2 : 3 : 5 : 5-*Pentamethylhexane*-3-*carboxylic Acid*. Ten recrystallisations of the brucine salt (m. p. 116—118°) from 75% aqueous acetone yielded a product which on decomposition afforded an optically inactive acid. The cinchonidine salt, m. p. 153°, was recrystallised four times from dilute alcohol and then decomposed with mineral acid, to yield a partially resolved acid, m. p. 135°, $[\alpha]_D^{18}$ +2·7°. The cinchonine salt, on the other hand, afforded an acid of $[\alpha]_D^{18}$ +3·1° after only three recrystallisations. Accordingly, cinchonine (112 g.) was gradually added to a boiling solution of the acid (75 g.) in ethanol (1 l.), and the liquid diluted with more ethanol until dissolution was complete, the total volume then being 4 l. On cooling, unchanged cinchonine (35 g.) was deposited. After filtration the solution was boiled and water added until crystallisation commenced. When cold, the liquid afforded a salt, m. p. 220—225°, $[\alpha]_D^{18}$ +143°. Eleven more recrystallisations from 50% aqueous ethanol yielded the pure *cinchonine* 2 : 2 : 3 : 5 : 5-*pentamethylhexane*-3-*carboxylate*, m. p. 215° (10 g.) (Found: C, 74·9; H, 9·3; N, 6·0. $C_{31}H_{46}O_3N_2$ requires C, 75·3; H, 9·4; N, 5·7%), whence was obtained a (+)-acid, m. p. 130°, $[\alpha]_D^{18}$ +23·8° (in ethanol).

3-*Methylhexane*-3-*carboxylic acid*. Attempted syntheses of this acid employing published methods [10] were unsuccessful; consequently Doering and Wilberg's procedure starting from substituted acetoacetic esters [11] was adopted. Ethyl propylacetoacetate was best methylated by using potassium *tert.*-butoxide as catalyst. Ethyl α-methylvalerate, b. p. 108—112°/13 mm. (53%) (Found: C, 65·0; H, 10·2. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%), so obtained was reduced with Raney nickel in ethanol, affording ethyl α-(1-hydroxyethyl)-α-methylvalerate, b. p. 104—106°/12 mm. (65%), and unchanged keto-ester. The hydroxy-ester (50 g.) was dehydrated by phosphoric oxide (50 g.) yielding impure ethyl 3-methylhex-1-ene-3-carboxylate, b. p. 83—85°/19 mm. (60%) (Found: C, 69·0; H, 11·1. Calc. for $C_{10}H_{18}O_2$: C, 70·5; H, 10·7%). Hydrogenation of the unsaturated compound (250 g.) with Raney nickel at 5 atm. furnished ethyl 3-methylhexane-3-carboxylate, b. p. 73—75°/13 mm. (227 g., 85%). The corresponding acid, b. p. 114—117°/11 mm., was obtained (yield, 80%) by hydrolysis with concentrated methanolic potassium hydroxide (Found: C, 66·7; H, 11·1. Calc. for $C_8H_{16}O_2$: C, 66·6; H, 11·2%). A mixture of the acid (22 g.) and thionyl chloride (30 g.) was kept at room temperature for 12 hr.: distillation yielded the acid chloride, b. p. 68—69°/17 mm. (22 g., 90%).

Resolution: Brucine was used but later experience suggested that it was probably not the best choice. The acid (151 g.) was boiled for 30 min. under reflux with brucine (412 g.) and acetone (500 c.c.), and the product (532 g.) then precipitated with light petroleum (b. p. 60—80°). The salt was very soluble in ethyl acetate, forming viscous solutions when concentrated. In the first instance methanol was used for recrystallising it but after 19 recrystallisations the acid recovered from the sample had a specific rotation of only 6° and consequently a 1 : 2 mixture of ethyl acetate and light petroleum (b. p. 60—80°) was employed, about two-thirds of the salt separating after each operation. Owing to the relatively low yield of salt and the large number of recrystallisations required (about 40 in all), a systematic procedure such as is described in " Organic Reactions " [12] was followed, the progress of the resolution being followed by measuring the rotation of the free acid. The final brucine salt, m. p. 70—71°, yielded optically pure (+)-3-methylhexane-3-carboxylic acid, $[\alpha]_D^{18}$ +19·7° (in 95% ethanol).

Friedel–Crafts Reactions.—In these reactions, the benzene and aluminium chloride were of the quality employed in the kinetic work.[13] " AnalaR " anisole was dried over anhydrous sodium sulphate and redistilled.

(i) Inactive phenyl-*p*-tolylacetyl chloride (from 2 g. of acid) in anisole (5 c.c.) was added

[10] Haller and Bauer, *Compt. rend.*, 1909, **148**, 130; Hauser and Breslow, *J. Amer. Chem. Soc.*, 1940, **62**, 2457; Lester and Proffitt, *ibid.*, 1949, **71**, 1877.
[11] Doering and Wilberg, *ibid.*, 1950, **72**, 2608.
[12] *Org. Reactions*, Vol. 2, p. 400.
[13] Grundy, Hsü, and Rothstein, *J.*, 1956, 4558.

slowly to a stirred suspension of aluminium chloride (2 g.) in the same solvent (25 c.c.) at 0°. The mixture was stirred for 1 hr. at room temperature and for 1 hr. at 50—60°. The resulting *p*-methoxyphenyl 4-methyl-α-phenylbenzyl ketone (2·3 g.) crystallised from dilute ethanol in a form of m. p. 134° (Found: C, 83·6; H, 6·3. Calc. for $C_{22}H_{20}O_2$: C, 83·5; H, 6·4%). This ketone, as previously prepared by Rothstein and Saville,[3] had m. p. 107—108° but the two did not depress each other's melting points on admixture and their infrared spectra (in KCl) were identical. Repeated crystallisations from various solvents left their respective m. p. unchanged.

(ii) Reaction (i) was repeated with (+)-phenyl-*p*-tolylacetyl chloride. In two experiments the yield of *inactive* ketone, m. p. 134°, was 2·3 g. and 2·1 g. The products were identical with that described above.

(iii) Reaction (i) was repeated both with inactive and with (+)-α-*p*-chlorophenyl-α-phenylacetyl chloride. In both cases the inactive ketone was obtained. *3-Chloro-α-phenylbenzyl* p-*methoxyphenyl ketone* crystallised from dilute alcohol in needles, m. p. 141° (2·1 g., 77%) (Found: C, 75·4; H, 5·3; Cl, 10·4. $C_{21}H_{17}O_2Cl$ requires C, 75·0; H, 5·1; Cl, 10·6%).

(iv) Inactive α-phenyl-α-*p*-tolylpropionyl chloride was prepared from the acid (2 g.) and excess of thionyl chloride, the unchanged reagent being removed in a vacuum. The reaction with anisole afforded p-*methoxyphenyl* 1-*phenyl*-1-p-*tolylpropyl ketone*, m. p. 105° (1 g.) (from ethanol) (Found: C, 83·8; H, 6·3. $C_{23}H_{22}O_2$ requires C, 83·6; H, 6·7%).

(v) Similarly (−)-α-phenyl-α-*p*-tolylpropionyl chloride (2 g.) yielded (−)-*p*-methoxyphenyl α-phenyl-α-*p*-tolylpropyl ketone, m. p. 105°, $[\alpha]_D^{18}$ −12·1° (in chloroform) (1·1 g.).

(vi) The above (−)-acid chloride (from 1·2 g. of acid), dissolved in benzene (5 c.c.), was added to a stirred suspension of aluminium chloride (1·8 g.) in benzene (25 g.). The product had a yellow-blue fluorescence in ethyl acetate and on fractionation yielded two liquids: Fraction (*a*), b. p. 100—102°/0·05 mm. (0·30 g.), was mainly hydrocarbon. The b. p. was considerably higher than that of phenyl-*p*-tolylmethane (b. p. 85—86°/0·04 mm.) and of diphenylethane (b. p. 97—98°/0·2 mm.), indicating the possible presence of 1 : 1-diphenyl-1-*p*-tolylethane (Found: C, 91·6; H, 7·1. Calc. for $C_{21}H_{20}$: C, 92·6; H, 7·4%). The infrared spectrum differed considerably from that of diphenylmethane, diphenylethane, and phenyl-*p*-tolylethane. The substance was optically inactive. Fraction (*b*) was an optically inactive ketone of indefinite b. p. (160—175°/0·05 mm.), having strong CO absorptions at 1730 and 1718 cm.$^{-1}$ (Found: C, 86·9; H, 6·8%).

Condensations of **2 : 2 : 3 : 5 : 5-*pentamethylhexane*-3-*carbonyl chloride*** (vii—x). (vii) A solution of the acid chloride (10 g., 0·046 mole) in anisole (50 c.c.) was cooled to 0° and aluminium chloride (10 g., 0·075 mole) was gradually added by means of a hopper. Carbon monoxide was vigorously evolved (1010 c.c., 95%). The mixture afforded three products all of which contained a methoxyphenyl group, *viz.*: (*a*) possibly *p-tert.*-butylanisole, b. p. 52—53°/0·1 mm. (5·2 g.) (Found: C, 80·1; H, 10·2. Calc. for $C_{11}H_{16}O$: C, 80·4; H, 9·8%), (*b*) possibly 3-p-*methoxyphenyl*-**2 : 2 : 3 : 5 : 5-*pentamethylhexane***, b. p. 67—68°/0·1 mm. (2·9 g.) (Found: C, 81·8; H, 11·1. $C_{18}H_{30}O$ requires C, 82·4; H, 11·5%) (no infrared CO absorption), and (*c*) a low-melting solid, b. p. 108°/0·1 mm. (0·30 g.) (strong CO absorption at 1684 cm.$^{-1}$), analysis corresponding to 1-tert.-*butyl*-**1 : 3 : 3-*trimethylbutyl methoxyphenyl ketone*** (Found: C, 79·0; H, 10·2. $C_{19}H_{30}O_2$ requires C, 78·6; H, 10·4%).

(viii) The above experiment was repeated with 2 g. of the (+)-acid chloride. All the products obtained were inactive, but the trace of ketone obtained was in any case too small for reliable optical measurements.

(ix) The fractions obtained when the acid chloride (10·5 g.) in benzene (50 c.c.) was mixed with aluminium chloride at room temperature were as follows:

		Found (%)				Found (%)	
Fraction	B. p./mm.	C	H	Fraction	B. p./mm.	C	H
1	51°/12	83·8	12·3	2	55°/12	86·7	12·2
3	72°/12	85·2	11·7	4	93°/12	81·7	12·6
5	115°/12	80·1	11·5				

The last three fractions had appreciable CO absorptions, at: 1759 and 1715 cm.$^{-1}$; 1786 and 1695 cm.$^{-1}$; and 1783 and 1698 cm.$^{-1}$ respectively. The first peak was relatively more intense than the second except in the last case where the reverse was true.

(x) Aluminium chloride (2 g., 0·015 mole) was stirred with phenol (5 g., 0·05 mole) in benzene

(10 c.c.) at room temperature until the liquid was homogeneous. The acid chloride (2 g., 0·009 mole) in benzene (3 c.c.) was then added and stirring continued for 2 hr. Little gas was evolved and the principal product was *phenyl* 2 : 2 : 3 : 5 : 5-*pentamethylhexane*-3-*carboxylate*, b. p. 110°/0·2 mm. (2 g., 85%) (Found: C, 78·1; H, 10·1. $C_{16}H_{26}O_2$ requires C, 78·2; H, 10·2%) [no OH bands; ester-CO at 1742 (s) cm.$^{-1}$]. The (+)-acid chloride similarly furnished (+)-phenyl 2 : 2 : 3 : 5 : 5-pentamethylhexane-3-carboxylate (80%), b. p. 99—100°/0·05 mm., $[\alpha]_D^{18}$ +24·3°, +24 8° (in ethanol) (separate experiments).

Condensations of 3-*methylhexane*-3-*carbonyl chloride* (xi—xiii). (xi) The inactive acid chloride (4 g., 0·025 mole) in anisole (5 c.c.) was added slowly to a stirred suspension of aluminium chloride (4 g., 0·03 mole) in the same solvent (10 c.c.) cooled in an ice-bath. The liquid was then stirred for 1 hr. at room temperature and for a further hour at 50—60°. This mixture afforded inactive 3-p-*methoxybenzoyl*-3-*methylhexane*, b. p. 120—122°/0·6 mm. (4·6 g., 74%) (Found: C, 77·1; H, 9·6. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%).

(xii) (+)-3-Methylhexane-3-carboxylic acid (2 g.) was converted into the acid chloride by leaving it for 12 hr. at room temperature with excess of thionyl chloride. The residual product after removal of unchanged reagent yielded (+)-3-*p*-methoxybenzoyl-3-methylhexane, b. p. 118°/0·5 (yields 31% and 34% in two similar experiments), $[\alpha]_D^{18}$ +14·3°, 14·7°. Fission of the ketone with ethanolic potassium hydroxide afforded *p*-anisic acid, m. p. 184° (Found: C, 63·1; H, 5·4. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%).

(xiii) The inactive acid chloride (2 g.) was similarly condensed with benzene, yielding a hydrocarbon, b. p. 95°/10 mm. (1·5 g.). Analysis corresponded to di-(1-ethyl-1-methylbutyl)-benzene rather than to 3-methyl-3-phenylhexane (Found: C, 87·2; H, 12·5. Calc. for $C_{20}H_{34}$: C, 87·6; H, 12·4%), but the b. p. was only slightly higher than that found for the latter prepared from 3-methylheptan-3-ol,[14] b. p. 93—95°/8 mm. (Found: C, 89·0; H, 11·3. Calc. for $C_{13}H_{20}$: C, 88·6; H, 11·4%). There was a vigorous liberation of carbon monoxide during this reaction. Two similar experiments with the (+)-acid chloride prepared from the (+)-acid (2 g.) afforded the same inactive hydrocarbon (45%, 37%). These experiments were carried out at room temperature and heat was not used to complete the reaction.

The Chemical Society is thanked for a Research Grant (E. R.) and the Department of Scientific and Industrial Research for a Maintenance Allowance (to W. B.). We are also indebted to Messrs. Alchemy, Ltd., London, for generous gifts of " Siccatic Acids, A and B " ($\gamma\gamma$-dimethyl-α-*neo*pentylvaleric and αββ-trimethyl-α-*neo*pentylbutyric acid).

The University, Leeds. [*Received, May 20th,* 1958.]

[14] Huston and Hsiu, *J. Amer. Chem. Soc.*, 1936, **58**, 439.

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774. *The Virial Coefficients of Carbon Disulphide, Diethyl Ether, and* n-*Hexane.*

By G. A. Bottomley and C. G. Reeves.

The virial coefficients of carbon disulphide, diethyl ether, and *n*-hexane have been determined to very high precision in the reduced temperature range 0·53 to 0·74 by differential compressibility. The experimental work demonstrates very clearly that the *PV*–*P* isotherms are linear up to 70% of the saturation pressure. Details of the manometric apparatus are discussed.

The *PVT* behaviour [where *P* is the pressure (atm.), *V* the volume (cm.^{3}) occupied by 1 mole, and *T* the absolute temperature] of three vapours was examined with the same method and differential compressibility apparatus as for benzene.[1] A sample of the vapour confined over grease-free mercury in a Pyrex apparatus is brought to the same pressure (±0·0002 mm.) as a similarly confined reference sample of nitrogen. The separate volumes of the vapour and the reference gas are determined to 1 in 100,000 by methods involving only the weighing of mercury. The pressures of the vapour and nitrogen are

[1] Bottomley, Reeves, and Whytlaw-Gray, *Proc. Roy. Soc.*, 1958, *A*, **246**, 504.

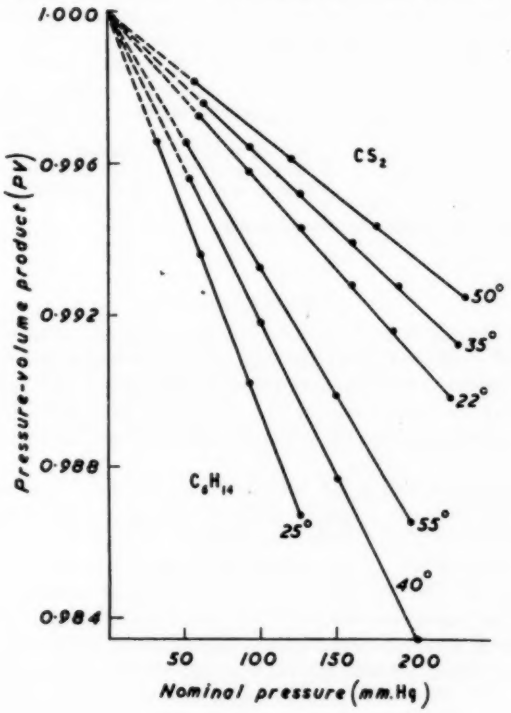
changed and re-balanced; the volume determinations are then repeated. After making the very slight allowance for the non-ideality of the reference gas these measurements permit the calculation of PV as a function of pressure for the vapour and so lead to the enumeration of virial coefficients.

Experimental

Materials.—Carbon disulphide. " AnalaR " material was repeatedly agitated with clean mercury until no further fouling of the interface occurred and then fractionally distilled in nitrogen from phosphoric oxide and mercury.

Diethyl ether. " AnalaR " material was shaken at intervals with 10% aqueous potassium hydroxide containing a small amount of potassium permanganate, washed with water, agitated

Fig. 1. *Pressure–volume product as function of pressure.*



with 10% aqueous ferrous sulphate slightly acidified, dried (Na_2SO_4), and fractionally distilled from sodium.

n-*Hexane.* Used as supplied by the Chemical Research Laboratories, Teddington, Middlesex (99·81 moles %).

The samples were then separately sealed without decomposition into vapour preparation lines controlled by mercury cut-offs. The carbon disulphide and *n*-hexane were dried by long-continued cycling over phosphoric oxide; the ether was stored as liquid over vacuum-distilled metallic sodium. Before use each sample was freed from entrained gases by repeated vacuum distillation at both −180° and −80° until Young's test (see following paper) was negative. Care is needed when carbon disulphide is solidified as the solid can easily shatter the glass container unless the crystals are grown upwards from the bottom of the specimen bulb. The vapour

pressures of the purified materials were measured to ±0·05 mm. Hg with a wide-bore manometer to provide the following comparison with values in the literature.[3]

Material	Obs. vapour pressure (mm.)	Reported vapour pressure (mm.)
CS_2	128·0 at 0°	127·3, 127·9, 128·0, 126·4, 127·0, 127·25
$C_4H_{10}O$	186·3 at 0°	186·1, 184·9, 185·3
C_6H_{14}	46·2 at 0°	45·45, 45·4

Conduct of an Isothermal Measurement.—The vapour, purified and degassed, was transferred to one side of the differential apparatus and opposed by nitrogen dried at −180°.[1] The individual PV products are reliable to 2 in 10^5 at all pressures used. As in the previous work,[1] the pressure of the nitrogen was measured at the highest pressure and then deduced for the subsequent lower pressures from the successive volumes of the nitrogen phase.

Results.—The virial coefficients (B) were computed from the slope of the PV–P line best fitting the observations after making the usual allowances for non-ideality of the nitrogen and the reduction of the pressure to standard conditions. Each expansion included measurements at four or more equally spaced pressures. The individual PV values differed from the mean lines by no more than 2 in 10^5: typical differences were: CS_2 (−0·2, −0·3, +0·8, −0·5), $C_4H_{10}O$ (+1·0, −2·0, +1·1, −0·7), C_6H_{14} (+0·9, −1·3, −0·2, +0·5) in parts per 10^5 of the PV value.

The final values of $-B$ (cm.^{3}/mole), with a probable error of ±3 cm.^{3}/mole, were:

CS_2	849 at 22·0°	748 at 35·0°	661 at 50·0°
$C_4H_{10}O$	1226 at 22·0°	1084 at 35·0°	950 at 50·0°
C_6H_{14}	1984 at 25·0°	1620 at 40·0°	1406 at 55·0°

Fig. 1 shows the working range of pressure used.

Discussion

Comparison with Related Work.—Direct PVT measurement. The values reported here for *n*-hexane and for diethyl ether at the highest temperatures overlap with the lowest temperature values reported by Lambert, Roberts, Rowlinson, and Wilkinson.[3] Though these authors estimate the probable error of their results as ±20 to ±100 cm.^{3}/mole and the values at various temperatures show considerable scatter, our values and theirs agree within these limits.

The higher-temperature values for *n*-hexane just overlap with the experiments of McGlashan and Potter;[4] if allowance is made for the alternative notations in use, our values clearly are distinctly less negative than theirs.

Values deduced from density. Much pioneer work has been done by R. Whytlaw-Gray and his collaborators on the possibility of obtaining virial coefficients by determining densities with the microbalance. This method has advantages in special cases, though it is far more sensitive to the purity of the material than the direct method. Casado, Massie, and Whytlaw-Gray[5] present work which leads to B values: diethyl ether −1211, carbon disulphide −658 cm.^{3}/mole at 22°. The agreement with ether is as perfect as the errors permit; the value for carbon disulphide (which is at present under re-examination by the microbalance method in these laboratories) is markedly anomalous. A similar disparity for benzene was resolved when adsorption errors were studied systematically in the two methods.

Values by indirect method. The second virial coefficient of a vapour can be deduced from the molar volume of the liquid, the calorimetric latent heat of vaporisation, and

[3] Timmermans, "Physico-chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[3] Lambert, Roberts, Rowlinson, and Wilkinson, *Proc. Roy. Soc.*, 1949. *A*, **196**, 113.
[4] McGlashan and Potter, Joint Conference of Thermodynamic and Transport Properties of Fluids. The Institution of Mechanical Engineers and the International Union of Pure and Applied Chemistry, July 1957.
[5] Casado, Massie, and Whytlaw-Gray, *Proc. Roy. Soc.*, 1952, *A*, **214**, 466.

vapour pressure as a function of temperature, if sufficiently accurate data are available.[6] Waddington and Douslin [7] have applied this method to *n*-hexane and give

$$B = -2270 + 6{\cdot}25 \times 10^5 T^{-1} - 1{\cdot}306 \times 10^{13} T^{-4}$$

as the relation between the second virial coefficient and the absolute temperature. The values from this equation at the temperatures of our experiments with *n*-hexane are −1825, −1634, and −1492; the agreement is far from impressive.

The results quoted above have been obtained at lower reduced temperatures (T/T_c), where the subscript c denotes a critical-point parameter, than those commonly employed. Fig. 2 shows reduced virial coefficients as a function of reduced temperature; the critical

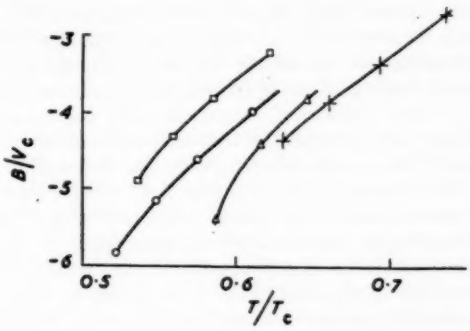


FIG. 2. *Reduced virial coefficient* (B/V_c) *as function of reduced temperature* (T/T_c).
□ Carbon disulphide.
○ Benzene, previous work (ref. 1).
△ *n*-Hexane.
\+ Diethyl ether.

data used are taken from Kobe and Lynn.[8] It is obvious that B/V_c is not a unique function for all substances and that errors of 20% can easily arise if it is assumed that a particular substance follows the general trend.

In the present work the PV–P line is linear to high accuracy, justifying the use of the equation

$$PV = \boldsymbol{R}T + BP/M$$

to represent the data, where M is the molecular weight. Some authors [4] recommend

$$PV = \boldsymbol{R}T + B'(1/V)/M$$

as being of greater theoretical significance. The present experimental data can equally well be handled on this basis since the volume of the system is determined at various pressures in each expansion. *PV versus* $1/V$ plots drawn from the observations appear very nearly linear when drawn on quarto graph paper.

If $PV = 1 + bP$, then $PV = 1 + (b/V)/(1 - b/V)$

and by binomial expansion

$$PV = 1 + b(1/V) + b^2(1/V)^2 + b^3(1/V)^3 \ldots\ldots$$

A typical value of b is −0·00006; over the working range of $(1/V)$ the term $(1/V)^2$ contributes some 0—4 parts per 10^5 to the PV values. At a nominal vapour pressure of 200 mm., $PV = 0{\cdot}988$ and $1/V = 202{\cdot}429$, so it follows that B' is smaller than B by

[6] Allen, Everett, and Penney, *Proc. Roy. Soc.*, 1952, *A*, **212**, 149.
[7] Waddington and Douslin, *J. Amer. Chem. Soc.*, 1947, **69**, 2275.
[8] Kobe and Lynn, *Chem. Rev.*, 1953, **52**, 117.

1·2%. We state firmly that the relative merits of PV–P and PV–$(1/V)$ plots cannot be established unless the experimental results and the reports include measurements of PV at several widely spaced pressures for each expansion.

Adsorption.—The mass of vapour contributing to the gas phase varied slightly with pressure because of the adsorption on the glass walls of the apparatus and on the mercury. The necessary slight allowances for the glass adsorption were made from Bottomley and Reeves's data,[9] but there is unfortunately no information on the adsorption of these vapours on mercury. The adsorption corrections are less serious than with benzene; the uncertainty cannot exceed 5 cm.^{3}/mole at most with the present apparatus.

Dilation of Apparatus.—During an experiment the apparatus was subjected to various pressure differences between interior and exterior which cause slight changes in the effective volume. No significant error arose in this way. Over the normal pressure range the volume change did not exceed 6 parts in 10^5 of the gas or vapour volume; the apparatus was symmetrical, so that volume changes and their consequences on one side were paralleled on the other; the rate of change of volume with pressure on the two sides has been measure accurately and found identical within satisfactory limits.

Static Electricity.—Some difficulty was caused by the unavoidable generation of static electricity through the movement of mercury over the Pyrex glassware which had been very thoroughly dried by repeated evacuation with the diffusion pump and by rinsing with nitrogen dried at −180°. The static electricity prevents the attainment of a stable pressure balance until some hours have elapsed after the movement of substantial amounts of mercury. If the observed anomalous pressures are due to static electricity producing electrostriction in the volume of the nitrogen or the vapour (though this is not the only possible explanation) then our apparatus with one gas phase subjected to an electrical potential gradient should prove a very direct method of investigation. None of the vapours examined showed any change in PV at constant pressure with time, so that under our conditions the materials are stable towards mercury, light, and static electricity. This apparently self-evident point is mentioned because it had been planned to study carbon tetrachloride. It was found that PV of a sample of highly purified carbon tetrachloride showed a steady fall of 10 parts per 10^5 for each redetermination at fixed pressure, and the mercury meniscus in the null manometer became foul at the contact with the glass. This behaviour is undoubtedly due to the rupture of the carbon tetrachloride molecule by static electricity to form carbon and mercurous chloride.

Capillarity.—The key operation of the experiments was the adjustment of the pressures on the two sides of a null manometer fitted with tungsten reference points. The setting of a mercury surface to a tungsten point can be made reproducible [10] to within 0·0002 mm., but this does not guarantee that the pressure equality of the two sides is so good. The reference points were first brought to the same horizontal plane by tilting the null manometer until, with both sides highly evacuated, the mercury surfaces set simultaneously to each tungsten point. With 35 mm. tubing it is certain that no possible variation of meniscus height and capillary depression can adversely influence the setting operation. When, as in the working experiments, the null manometer contains nitrogen on one side and a vapour at perhaps 70% saturation on the other, various possibilities for error exist. The vapour is adsorbed on the mercury surface, lowers the surface tension, and reduces the capillary depression, but cannot affect the depression by more than 0·001 mm. with 35 mm. bore tubes even if the meniscus is made horizontal. Above room temperature the vapour pressure of the mercury is appreciably higher than the permissible error in manometry, so it must be ensured that both the vapour and the nitrogen, in which diffusion proceeds at different rates, become fully saturated with mercury vapour before a pressure balance is attempted. Because of the need to allow 24 hr. to elapse to disperse static electricity, we have not found any evidence of difficulty from this potential error.

[9] Bottomley and Reeves, *Trans. Faraday Soc.*, 1957, **53**, 1455.
[10] Bottomley, *J. Sci. Instr.*, 1958, **35**, 254.

Manometric Errors.—Rowlinson and his co-workers [11,12] have drawn attention to the possible detrimental effect of mercury vapour in substances under *PVT* examination at moderate and high pressures and have shown experimentally that the presence of a vapour enhances the solubility of mercury in the gas phase by as much as 35% in certain circumstances. That this effect does not influence our experiments has been demonstrated as follows: with the thermostat at 22° (mercury-vapour pressure 0·0014 mm.) nitrogen was admitted to one side of the null manometer and diethyl ether to the other, the two gas phases being connected by a long capillary tube. The manometer system was then tilted until the tungsten points set simultaneously to the mercury surfaces. This setting does not occur with the points horizontal because of the slightly different hydrostatic heads of the vapour and nitrogen in the dead spaces, a fact which demontrates the extreme sensitivity of the point settings. The null manometer was maintained at the same level, the thermostat temperature raised to 57° (mercury-vapour pressure 0·020 mm.) and the filling repeated. The null manometer showed no pressure difference. It follows that the vapour pressures of mercury in the two gas phases at 57° are identical to $\pm$0·001 mm. at worst, and that the enhanced solubility effect does not amount to more than 5% of the vapour pressure of mercury.

There is another manometric error. The null manometer system permits adjustment to pressure equality at the level of the tungsten points but not at the level of the centre of gravity of the gas phase. The hydrostatic head between the level of the tungsten points and the centres of gravity is not the same because the gases have different density. Furthermore, as the gas phases are expanded during an experiment the disparity between the level of the null manometer and the centre of gravity changes. Elementary calculation from the vertical distribution of a gas in a gravitational field shows that the effects are just at the limit of precision of our experimental technique; with a vapour as dense as perfluoromethyl*cyclo*hexane the corrections would be significant.

The capillary effect of the tungsten rod which protrudes through the mercury meniscus (within 1 mm. of the dead-space wall) was of some practical importance. To test the " figure " of a meniscus of 35 mm. diameter interference fringes were formed with sodium light between the mercury and an optical flat partially obscured with chemically deposited lead sulphide to increase the contrast. An obstacle corresponding to the tungsten rod was then inserted through the meniscus and the limits of distortion of the fringes observed visually. The capillary disturbance extended from the rod much further than might be supposed but did not materially affect the centre of the 35 mm. diameter meniscus. By the same test it was clear that the curvature of the central 10 mm. of the meniscus was little more than 1 wavelength, so that exact centering of the tungsten reference point was not required.

AKERS RESEARCH LABORATORIES, IMPERIAL CHEMICAL INDUSTRIES LIMITED,
THE FRYTHE, WELWYN, HERTFORDSHIRE. [*Received, June 17th*, 1958.]

[11] Jepson and Rowlinson, *J. Chem. Phys.*, 1955, **23**, 1599.
[12] Jepson, Richardson, and Rowlinson, *Trans. Faraday Soc.*, 1957, **53**, 1586.

XUM

775. *The Virial Coefficients of* cyclo*Hexane, Carbon Disulphide, and Carbon Tetrachloride Vapours.*

By G. A. Bottomley and T. A. Remmington.

The densities of the vapours of *cyclo*hexane, carbon disulphide, and carbon tetrachloride relative to that of nitrogen have been determined by the silica-suspension microbalance. The virial coefficients have been deduced by a comparison between the observed density and that calculated from the atomic weights. Pressures were measured on a manometer with an internal reference grid: experimentally determined corrections for adsorption were applied. Purification of the materials limited the precision.

The microbalance technique for the determination of virial coefficients previously used for benzene [1] has been applied to three other vapours. The separate pressures are determined at which the vapour and nitrogen cause a quartz-fibre suspension microbalance to take up a particular balancing position equivalent to a definite density (g./ml.). If the equation of state for the vapour be represented by

$$PV = \boldsymbol{R}T + BP/M \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

[where P is the pressure (atm.), V the volume (cm.^{3}) occupied by 1 mole, and T the absolute temperature], then the corresponding density is $M/(\boldsymbol{R}T/P + B)$ g./ml. For two different gases (1 and 2) brought to the same density

$$B_2 = \frac{\boldsymbol{R}T}{P_2}\left[\left(\frac{M_2P_2}{M_1P_1}\right)\left(1 + \frac{P_1B_1}{\boldsymbol{R}T}\right) - 1\right] \quad . \quad . \quad . \quad . \quad . \quad (2)$$

so that the virial coefficient of the vapour (B_2) can be deduced from the exact molecular weights (M_1 and M_2), the balancing pressures (P_1 and P_2) (atm.) and the virial coefficient of the reference gas, B_1. Though the determination of the virial coefficient is thus reduced to the measurement of two pressures, there remain formidable difficulties of technique.

Experimental

Materials.—cyclo*Hexane.* Used as obtained from Bureau International des Étalons physico-chimiques, Brussels.

Carbon disulphide. " AnalaR " material was repeatedly shaken with clean mercury until no further darkening of the interface occurred, then distilled from mercury. The product was refluxed over phosphoric oxide and mercury in nitrogen and then slowly fractionated through a Dixon-ring column. The middle fraction was selected, though the boiling point was constant (±0·05°) throughout.

Carbon tetrachloride. Chlorine from a cylinder was bubbled into the " AnalaR " reagent until a strong yellow colour was present; the system was irradiated by direct sunshine for 8 hr. and left for 100 hr. in the dark. Excess of chlorine was removed with 10% potassium hydroxide, and then distilled water. The sample was then refluxed with 10% potassium hydroxide for several hours in a nitrogen atmosphere, washed with distilled water, and dried (Na_2SO_4, then P_2O_5). Finally it was fractionated from phosphoric oxide. The middle eight cuts boiled at 76·5° ± 0·05°, and gave indistinguishable refractive indices on a Pulfrich refractometer (±0·00002).

The purified samples were individually admitted to the nitrogen-purged lines of the apparatus, frozen in liquid nitrogen, and sealed with precautions to avoid contamination. For precautions with carbon disulphide see preceding paper (their neglect led to loss of the sample used in the density work with which it had been intended to determine the isotopic composition). The samples were desiccated *in situ* by phosphoric oxide. No special

[1] Bottomley, Remmington, and Whytlaw-Gray, *Proc. Roy. Soc.*, 1958, *A*, **246**, 514.

precautions were taken to avoid photochemical change as the laboratory was illuminated only by subdued artificial lighting. It was necessary to eliminate traces of non-condensable gases (nitrogen, oxygen, inert gases) and carbon dioxide, because of their effect on the density. 1 Part in 2500 of nitrogen in the *cyclo*hexane was equivalent to a 5% error in the virial coefficient. The materials were repeatedly distilled from trap to trap at −180° and −80° with frequent evacuation on the diffusion pump. No permanent gas could be detected at the tip of a 0·1 mm. bore tube when about 2 ml. of the vapour was compressed by an advancing surface of the condensed vapour (Young's test).

Nitrogen. This was a special sample in a cylinder provided by The British Oxygen Co. Ltd. from liquid-air fractionation. Details of its composition are given by Reeves and Whytlaw-Gray.[2]

Determination of the Balancing Pressures.—The gaseous pressures bringing the balance to equilibrium were determined by a Rayleigh manometer in which the uncertain setting of a cathetometer cross-wire on the vertex of a 40 mm. diam. mercury meniscus was replaced by a series of operations in which mercury surfaces were set to tungsten reference points. The reproducibility of the pressure measurements in this fashion was considerably better than the 0·01 mm. of conventional cathetometry. The gases and vapours were contaminated by mercury vapour because they were handled by mercury cut-offs or similar methods. To maintain a mercury-free condition in the balance case the entrance line was protected by a trap containing gold foil and granules and the interior of the balance case, with the exception of the portions required for observation, was covered with fired-on gold film. The balance case was never kept evacuated overnight, but when left unattended was always filled with nitrogen to near the balancing pressure to reduce the diffusion of mercury towards the balance.

If $\boldsymbol{R}$, T, M_1, and M_2 are regarded as exactly specified constants, then by numerical substitution into eqn. (2) it can be seen that the absolute density of the mercury, the gravitational and altitude corrections, and the absolute value of the length scale of the manometric system do not warrant consideration. In the conditions of the present experiments it is believed that the quantity (M_2P_2/M_1P_1), which is necessarily close to unity, is known to about 0·0001, corresponding to an error of some 2% on the final value of B.

The Microbalance and Adsorption.—The balance used was of greater sensitivity than that employed for benzene, partly because a larger buoyancy bulb was used, and partly because of a more critical adjustment of the centre of gravity and the use of suspension fibres of smaller diameter. [Time of swing, 24 sec. Weight sensitivity, $1{\cdot}038 \times 10^{-5}$ g./mm. of point movement. Pressure sensitivity, 0·0231 mm. of point movement/0·01 mm. of nitrogen pressure change.] With the optical system used, the balance could be adjusted to within 0·003 mm. The limiting factors in the manipulations were the determination of the balancing pressure and the inability to define and position the balance relative to an arbitrary zero.

Since the silica surface of the balance acquires an equilibrium state of adsorbed vapour whose mass contributes to the displacement torques, correction to the hypothetical state of no adsorption is required. The balance and bulb used in the density work were converted into an adsorption balance by puncturing the bulb and readjusting ($\pm 2 \times 10^{-5}$ g.) the silica weights, so that the inner and the outer surface of the bulb acted as the adsorbing area when exposed to various pressures and temperatures of the experimental vapours. Some isotherms so determined have been reported.[3] The deflection of the density balance due to adsorption on the outer surface of the closed bulb is assumed to be half that of the deflection of the adsorption balance by the adsorption on the open bulb under comparable vapour conditions. The following well-defined corrections (to be subtracted from the observed balancing pressure) were obtained: *cyclo*hexane, 0·022 mm. at 22°, 0·013 mm. at 35°; carbon disulphide, 0·003 mm. at 22°, 0·001 mm. at 35°; carbon tetrachloride, 0·011 mm. at 22°.

Results.—The Table summarises the accepted observations on each substance. Each pressure entry represents a separate filling and balancing operation. From the quoted mean pressures and pressure ratios, together with the standard values of the atomic weights C, 12·011; H, 1·0080; Cl, 35·457; N, 14·008; S, 32·066; the gas constant $\boldsymbol{R}$, 82·057 cm.³ atm. (T mole^{-1}); and the virial coefficients of nitrogen, −5·3 cm.³/mole at 22° and −2·9 cm.³/mole at 35° c, the following final values for the second virial coefficients (cm.³/mole) can be deduced: *cyclo*hexane −1600 at 22°, −1515 at 35°; carbon disulphide −646 at 22°, −582 at 35°; carbon

[2] Reeves and Whytlaw-Gray, *Proc. Roy. Soc.*, 1955, *A*, **232**, 173.
[3] Remmington and Whytlaw-Gray, *Trans. Faraday Soc.*, in the press.

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tetrachloride −1283 at 22°. (These values include the necessary Rayleigh correction for the volume change of the buoyancy bulb when exposed to various pressures.)

Compound	Temp. (° c)	Nitrogen pressure (mm. Hg at 0°)	Vapour pressure (mm. Hg at 0°) *	Ratio
C_6H_{12}	22	164·954	54·647	3·01852
		164·952	54·643	3·01870
		164·917	54·626	3·01900
		164·896	54·634	3·01818
		164·931	54·644	3·01826
	(Mean	164·930	54·639	3·01853)
	35	172·133	57·036	3·01798
		172·124	57·038	3·01770
		172·127	57·030	3·01819
		172·051	57·024	3·01716
	(Mean	172·109	57·032	3·01776)
CS_2	22	164·968	60·575	2·72338
		164·972	60·561	2·72408
		164·926	60·567	2·72305
		164·975	60·567	2·72386
		164·986	60·574	2·72372
	(Mean	164·965	60·569	2·72362)
CS_2	35	172·184	63·227	2·72324
		172·159	63·207	2·72375
		172·134	63·206	2·72340
		172·147	63·226	2·72275
		172·219	63·251	2·72277
	(Mean	172·169	63·223	2·72318)
CCl_4	22	164·995	29·988	5·50203
		164·998	29·980	5·50359
		164·993	29·983	5·50287
		164·939	29·979	5·50181
		165·034	29·985	5·50390
		165·037	29·993	5·50254
	(Mean	164·999	29·985	5·50279)

* Includes adsorption correction.

Judged from the self-consistency of the separate ratios there appears to be good ground for assessing the error in B as about 2% .

Discussion

Comparison with Other Work.—cyclo*Hexane.* The present values are consistent (±100 cm.³/mole) with the data in the range 42—75° c by Waelbroeck [4] and 50—130° c by Lambert, Roberts, Rowlinson, and Wilkinson.[5] The precision of all the data is limited and an exhaustive re-examination of *cyclo*hexane over a wide temperature range is urgently required. With a different balance, probably less reliable, we obtained −1523 cm.³/mole at 35°, but −1663 at 22°, from 18 ratio determinations of the same self-consistency as those shown in the Table.

Carbon disulphide. Bottomley and Reeves,[6] using our material, determined the second virial coefficient at several temperatures with a precision differential compressibility apparatus and quote −849 and −748 cm.³/mole at 22° and 35°. It is impossible to disguise the gross discrepancy between the current work and these figures. Casado, Massie, and Whytlaw-Gray [7] by the microbalance method found B at 22° to be −658 cm.³/mole. The direct compressibility method is relatively insensitive to the absolute purity of the substance: 5% of nitrogen is required to produce a 5% error in B, in contrast to 0·04% in the microbalance method. It is possible that the samples are not free from carbon dioxide, but we have not yet devised a satisfactory chemical method of removing it.

Carbon tetrachloride. Casado, Massie, and Whytlaw-Gray [7] with the microbalance method gave A_2 as 0·0457 at 22°, and hence $B = -1107$ cm.³/mole. Lambert, Roberts, Rowlinson, and Wilkinson [5] studied the virial coefficient between 44° and 80°, but commented that it was impossible to make measurements with carbon tetrachloride above 80° c, as the vapour attacked the mercury in the burette, and that the measurements at lower temperatures may be in error for the same reason. Francis and McGlashan [8] carried out further measurements at 42—70°, obtaining results largely concordant with those of

[4] Waelbroeck, *J. Chim. phys.*, 1957, **54**, 710.
[5] Lambert, Roberts, Rowlinson, and Wilkinson, *Proc. Roy. Soc.*, 1949, *A*, **196**, 113.
[6] Bottomley and Reeves, preceding paper.
[7] Casado, Massie, and Whytlaw-Gray, *Proc. Roy. Soc.*, 1952, *A*, **214**, 466.
[8] Francis and McGlashan, *Trans. Faraday Soc.*, 1955, **51**, 593.

Lambert and his co-workers, but markedly divergent at the higher temperatures from the earlier work of Eucken and Meyer.[9] The value suggested by an extrapolation of the results at 40—80° is −1780 cm.^{3}/mole.

Static Electricity.—The involuntary generation of static electricity by the movement of the gases in the apparatus and the mercury surfaces in the various cut-offs causes considerable difficulty because the microbalance, being of highly insulating silica, acquires and retains charges for long periods and assumes spurious equilibria due to the electrical interactions. To minimise the errors from this cause, the gas, vapour, and mercury manipulations were carried out very slowly and the approach of the balance to equilibrium was followed for several hours before a final setting was attempted. The gold-plated interior of the balance case provided a high conductance and a large capacitance, but did not prevent trouble with static electricity.

Various suggestions have been made to reduce the trouble: a small radioactive source in the balance case to maintain an ionising atmosphere; radioactive ^{203}Hg at low concentration in the ordinary mercury and therefore in the gas phase; the provision of nearly transparent but electrically conducting films on all the glass interior surfaces by either chemical deposition of lead sulphide or treatment when hot with stannous chloride fumes. Trial experiments along these lines have been made.

With carbon tetrachloride vapour [10] there is also a chemical change due to the rupture of CCl_4 in the presence of mercury:

$$CCl_4 + 4Hg \longrightarrow \text{Various intermediates such as } C_2Cl_6 \longrightarrow 2Hg_2Cl_2 + C$$

Manifestations of this reactivity are seen in annular " tide-marks " in mercury manometers and the tendency of McLeod gauges to show " sticking mercury." Bottomley and Reeves [6] were unable to measure the virial coefficient of carbon tetrachloride over mercury because of this interference. The loss of vapour in an expansion amounted to 20—30% of the effect sought. This behaviour casts doubt on the accuracy of the measurements reported by Lambert *et al.* and Francis and McGlashan.

General Discussion.—The microbalance values for the present three substances, whilst evidently of the correct magnitude, do not warrant reliability as great as that suggested by the reproducibility of the balancing ratios. Two factors play a considerable part in this indefiniteness, the purity of the material, and the adsorption corrections. Because of the extraordinary sensitivity of the density balance, the purification of the working materials becomes a major research in itself, and we suggest that such discrepancies as do occur between different balances and different workers represent minor differences in purity of the working materials rather than any defect of the method as such. With carbon disulphide the isotopic variation of sulphur may be significant because of its effect on the assumed molecular weight. Though every care has been taken in the assessment of the adsorption effects, it still remains possible that the basic assumption, equal adsorption on the inner and outer surfaces of the silica bulb, is to some degree unjustified. Given adequate time and facilities there is no reason to doubt that the density balance method could be made considerably more reliable: as a practical proposition the direct measurement method, when it is carried out with suitable refinements to obtain a precision of 10 cm.^{3}/mole or better, is superior. With benzene, which has been examined [11] by both microbalance and compressibility methods in several laboratories, there is substantial agreement amongst all the data.

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THE FRYTHE, WELWYN, HERTS. [*Received, June 17th*, 1958.]

[9] Eucken and Meyer, *Z. phys. Chem.*, 1929, *B*, **5**, 452.
[10] Bottomley and Reeves, *Trans. Faraday Soc.*, 1957, **53**, 1455.
[11] Bottomley, Reeves, and Whytlaw-Gray, *Proc. Roy. Soc.*, 1958, *A*, **246**, 504.

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776. *Reactions and Stability of Chabazite-like Phases. Part I. Ion-exchanged Forms of Natural Chabazite.*

By R. M. Barrer and D. A. Langley.

The effects of heat upon cation-exchanged forms of chabazite have been investigated by differential thermal analysis, thermogravimetry, and *X*-ray diffraction. Eleven cation-exchanged forms of a rather siliceous chabazite having a silica : alumina ratio a little above 5, and the temperature interval 20° to ~1100°, were used. The influence of the cation on thermal stability was in the order Li < Na < K < Rb < Cs, and on water retentivity in the order Li > Na > K > Rb. Bivalent ions show greater retentivity for comparable radii than do univalent ions. In several instances loss of water occurred in more than one stage.

Besides glassy products, decomposition of the parent lattice yielded quartz in a number of instances, also β-eucryptite, leucite, and the hydrogen form of chabazite.

The synthetic mineral-type compounds grown in these laboratories [1] include a range of phases related in structure to chabazite–gmelinite minerals.[2,3] They include a group of potassium aluminosilicates characterised by a variable alumina : silica ratio ranging from 1 : 2·3 to 1 : 4·15. Natural chabazites may also vary in their alumina : silica ratios, but on the whole are more siliceous than the potassium aluminosilicates referred to above, while in the naturally occurring crystals the cations present are sodium and calcium. Also more siliceous phases related to the chabazite-gmelinite family of zeolites have been synthesised,[4,3] which contain only sodium as cation. It has become apparent therefore that a wide variety of compounds based on the chabazite-type of structure can be synthesised, in which the synthetic phases differ appreciably from their naturally occurring analogues. In the present paper an account will be given of the reactions and reactivity of various cation-exchanged forms of a natural rather siliceous chabazite, as revealed by differential thermal analysis, thermogravimetry, and *X*-ray diffraction. In later papers, a similar study of the synthetic potassium chabazite-like phases will be given, and of the hydration of members of the chabazite–gmelinite group of zeolites.

X-Ray powder photography has been used by Milligan and Weiser [5] in a systematic study of dehydration and stability of zeolites and hydrous oxides. Zveshnikova and Kuznetsov [6] have investigated relations between kaolinites and certain fibrous zeolites, using differential thermal analysis, and Koizumi [7] and Koizumi and Kiriyama [8] have examined dehydration of a considerable number of zeolites by use of *X*-rays and differential thermal analysis. Koizumi reported that four groups of zeolites could thus be distinguished. From differential thermal analysis of natrolite, scolecite, and mesolite Peng [9] concluded that in certain of these zeolites the water molecules may be arranged in groups having different volatilities. Such a view accords with *X*-ray structure determinations for these species.[10]

Experimental

Apparatus.—The equipment for differential thermal analysis was based on that used by Mackenzie.[11] The three main sections (furnaces, recorder unit, and control unit) were connected by two cables, one carrying the power connections and the other the thermocouple

[1] Barrer, *Trans. Brit. Cer. Soc.*, 1957, **56**, 155.
[2] Barrer and Baynham, *J.*, 1956, 2882, 2892.
[3] Barrer and Bultitude, unpublished work.
[4] Breck, Linde Air Products Co., personal communication
[5] Milligan and Weiser, *J. Phys. Chem.*, 1937, **41**, 1029.
[6] Zveshnikova and Kuznetsov, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1946, 25.
[7] Koizumi, *Mineralog. J. (Mineralog. Soc. Japan)*, 1953, **1**, 36.
[8] Koizumi and Kiriyama, *J. Geol. Soc. (Japan)*, 1953, **59**, 88; Sci. Report No. 2, Osaka Univ., 1953.
[9] Peng, *Amer. Mineralog.*, 1955, **40**, 834.
[10] Taylor, Meek, and Jackson, *Z. Krist.*, 1933, **84**, 373.
[11] Mackenzie, *Anal. Edafol. Fisiol. Veg.*, 1952, **11**, 159.

circuits. Ceramic furnace blocks and covers and small double cells were used. The cells contained the inert comparison specimen (ignited kaolin) and the reactive specimen, as well as the hot junctions of two thermocouples. Before introducing the reactive specimens into the cell, they were ground to pass 200 mesh and equilibrated at ~51% relative humidity by storage for ~4 days in a desiccator over a saturated solution of calcium nitrate.* The two cavities in the double cell were completely filled each time with the reactive sample and ignited kaolinite respectively. If there was insufficient of the reactive sample to fill the appropriate half of the double cell, it was mixed with ignited kaolin. A small metal plunger was used to pack the materials tightly and to reproduce the packing density as accurately as possible. The procedure of using equal volumes of sample and of reference material in the two halves of the cell provided the most reproducible temperature distribution throughout the specimen holder and thus gave a base line in the thermogram with the minimum of drift.

The apparatus was designed to provide a heating rate of 10° per min. up to about 1100° c. Any one of four identical furnaces could be heated and the rate was governed by the programme controller from a thermocouple embedded in the furnace core. The temperature of the inert reference material was recorded on a two-point recorder and the differential temperature on one of two instruments, (i) a potentiometric microvolt recorder or (ii) a direct reading millivolt recorder. The recorder systems were enclosed in an air thermostat. Most of the construction of this apparatus is due to Dr. J. S. Raitt, and to the workshop of the Chemistry Department, Aberdeen University.

TABLE 1. *Exchanges in chabazite.*

Exchanger	Solution	Strength of soln. (%)	Method	Temp.	Exchange (%)
Natural chabazite	NaCl	20	Steam-bath	90°	100
,,	$CaCl_2$	20	,,	90	100
Ca-chabazite	LiCl	20	,,	90	100
,,	KCl	20	,,	90	100
,,	NH_4Cl	20	,,	90	95·5
Na-chabazite	$SrCl_2$	20	,,	90	79
,,	$BaCl_2$	20	,,	90	90
Natural chabazite	$PbCl_2$	20	,,	90	~45
Ca-chabazite	RbCl	10	Sealed tube	110	100
,,	CsCl	10	,,	110	89·7
Natural chabazite	$Cu(NO_3)_2$	1	,,	25	50·6

TABLE 2. *Analysis of some ion-exchanged chabazites.*

	Molar proportions of constituents						
Mineral	SiO_2	Al_2O_3	CaO	BaO	SrO	Na_2O	H_2O
Natural chabazite	5·00	1·00	0·87	—	—	0·17	6·75
Na-chabazite	5·05	1·00	—	—	—	1·00	5·99
Ca-chabazite	5·11	1·00	0·97	—	—	—	6·91
Sr-chabazite	5·12	1·00	—	—	0·79	0·21	6·64
Ba-chabazite	5·15	1·00	—	0·90	—	0·10	6·17

The thermogravimetric apparatus included a furnace for heating the specimen operated by the same programme controller as were the furnaces of the apparatus for differential thermal analysis, and identical with these furnaces. Thus the heating rate was again 10° per minute. The specimen was suspended in a bucket by a very fine platinum filament from one arm of a suitably modified Stanton Model A.42 air-damped aperiodic balance. The wire was protected from draughts; the balance was shielded from heat from the furnace by sloping baffles.

For *X*-ray examination an HRX *X*-ray unit was employed. Hilger 9 cm. powder cameras were available. A copper anode bombarded by 38—39 kv electrons produced Cu-K_α and Cu-K_β characteristic radiation from which the Cu-K_β radiation was removed by means of nickel filters. Filaments were run at 15—20 milliamp. each, and exposure times of 4—6 hr. then normally sufficed for producing a good *X*-ray powder photograph.

Materials.—Natural chabazite from the Bay of Fundy, Nova Scotia, was used as parent material. From it ion-exchange products rich in Li, Na, K, Rb, Cs, NH_4, Ca, Sr, Ba, Pb, and

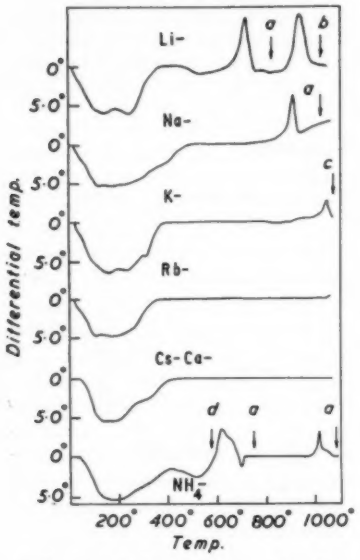
* The relative humidity of such solutions varies somewhat with ambient room temperature. However, in the small temperature interval involved this variation is small, and in this region the water sorption is moreover nearly independent of humidity, owing to the rectangular shape of the isotherms.

Cu were made. In all these preparations the aqueous chlorides were employed, except in the case of Cu-rich chabazite for which aqueous nitrate was the exchanging solution. Some details are summarised in Table 1, and full analyses of the original chabazite and of its Na, Ca, Sr, and Ba forms are in Table 2. In these analyses standard analytical procedures were employed.[12] The chabazite is seen to be rich in silica.

Results

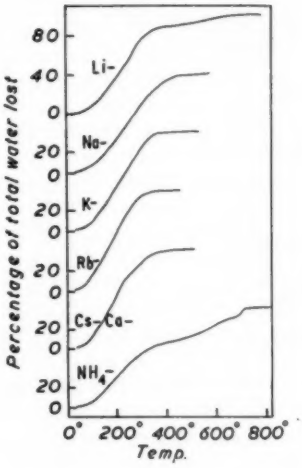
Thermograms and Thermogravimetric Curves.—The curves for differential thermal analysis of some of the ion-exchanged forms derived from natural chabazite are shown in Fig. 1. The major endotherm of Li-chabazite extends from room temperature to ~390°. It is followed by

Fig. 1. *Differential thermal analysis of ion-exchanged natural chabazites.* ($Al_2O_3 : SiO_2 = 1 : 5{\cdot}05$.)



a, Quartz; *b*, β-eucryptite; *c*, leucite; *d*, H-chabazite.

Fig. 2. *Thermogravimetric curves for ion-exchanged natural chabazites.* ($Al_2O_3 : SiO_2 = 1 : 5{\cdot}05$.)



a second, small endotherm starting at ~445° and merging into the first exotherm at about 660°. The peak temperatures of the two strong exotherms are at 731° and 955° respectively. In the Na-chabazite thermogram the two endotherms for the Li-form are replaced by one extending to 510°, and there is only one exotherm with a peak temperature at 921°. The endotherm of K-chabazite is completed at 408°, and the exotherm is less pronounced and occurs at 1064°. Rb-chabazite, which even approaching 1100° shows only the beginning of an exothermic process, has an endotherm terminating by 386°.

The four samples above each contain only one type of exchangeable cation, but the Cs-rich crystals contain $Cs^+ : Ca^{2+}$ ions in the ratio 18 : 1 (Table 1). At 250° the slope of the endotherm starts decreasing, and there is a small " plateau " which is completed by 460°. This final part of the curve can reasonably be attributed to the presence of the Ca ions and the water associated with them. The Cs-rich form showed no exotherm up to ~1100°.

In order to demonstrate that the endothermic sections of the differential thermal analysis curves were associated with water loss, the thermogravimetric curves of Fig. 2 were determined.

[12] *E.g.*, Harwood, " Practical Rock Analysis for Geologists," Imp. Coll. Science Technol., 1933; Vogel, " Quantitative Analysis," Longmans, London, 1948.

The first of these shows that water loss from Li-chabazite occurs in two stages, in agreement with the curve of Fig. 1. Fig. 2 shows also that completion of water loss has occurred at temperatures close to those at which the endothermal parts of the curves of Fig. 1 are completed.

The thermograms and thermogravimetric curves of Ca-, Sr-, and Ba-chabazite are shown in Figs. 3 and 4. The outstanding feature of Fig. 3 is the width of the endothermic parts. That for Ca-chabazite extends to 760° with a minimum at 220°. The corresponding thermogravimetric curve is smooth and slopes rather gently (Fig. 4). For Sr-chabazite, and particularly for Ba-chabazite, the water loss involves more than one stage. However, from Table 1 the numbers of ions present are respectively in the ratios Sr : Na = 79 : 42 and Ba : Na = 90 : 20. The sodium ions present may influence the differential thermal analysis and thermogravimetric curves. The endothermic section of the former curve of Ba-chabazite shows three parts, and the thermogravimetric curve shows that all are associated with some weight loss, so that the presence of sodium cannot explain the whole effect. The loss in weight in the last section of the endotherm is small and therefore it seems unlikely that the considerable heat effect can be due to water loss only.

FIG. 3.

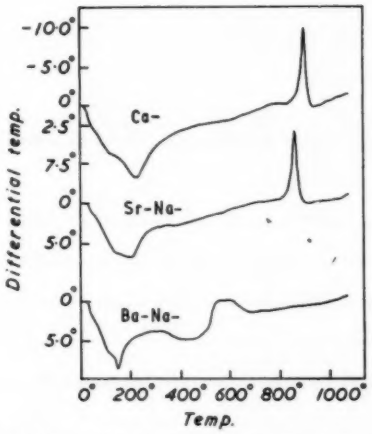
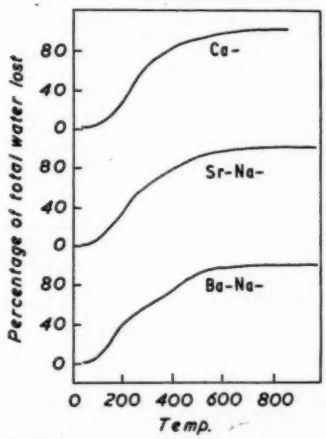


FIG. 4.



FIGS. 3 & 4. (Fig. 3) *Differential thermal analysis and* (Fig. 4) *thermogravimetric curves of natural chabazites rich in alkaline-earth metal ions.*

The differential thermal analysis curves for the chabazites enriched in copper and lead (Table 1) were also determined. Since some calcium and sodium were also present the curves are difficult to interpret and will not be considered further. There remain however the interesting curves for NH_4-chabazite (Figs. 1 and 2). Both are complex: in the endotherm water loss is also associated with loss of ammonia. There then follows an exothermic change with a peak at 614°, followed at once by a further endothermic process, giving a minimum at 692°. Finally, above 1000°, another exothermal reaction occurred. This thermogram is in some ways unique.

Structural Changes Associated with Differential Thermal Analysis.—*X*-Ray powder photographs were taken of the various ion-exchanged chabazites before and after heating to various temperatures in the furnaces of the differential thermal analysis apparatus. The heating rate was 10° per min., until the desired temperature was reached. Heating was then stopped and the material cooled rapidly in air. For temperatures below ~700° the powder was actually heated in very thin-walled Pyrex capillary tubes, which were quickly sealed after cooling. For temperatures above 700°, after the heat treatment the air-cooled powder was transferred as speedily as possible into the capillary tubes, which were again sealed. The *X*-ray powder photograph was then obtained. The maximum heating temperatures were at selected intervals between 20° and 1100°, these temperatures being chosen to follow changes revealed by the thermograms.

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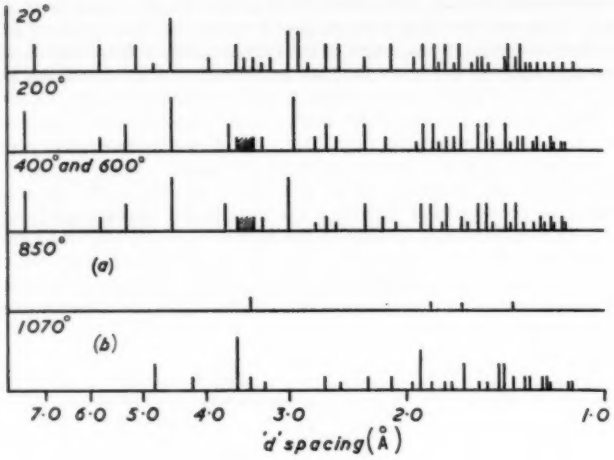

Fig. 5: Li-*chabazite.*

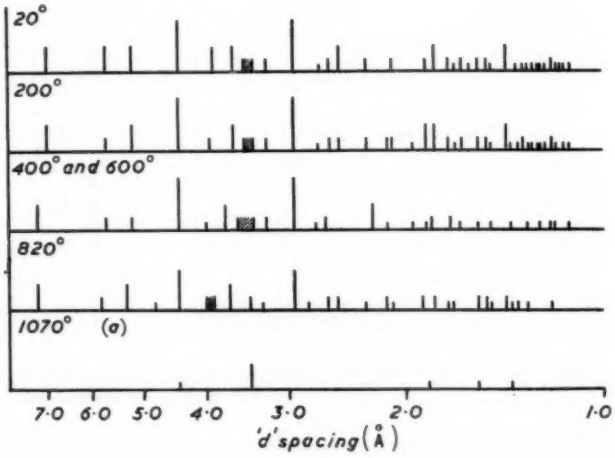

Fig. 6: Na-*chabazite.*

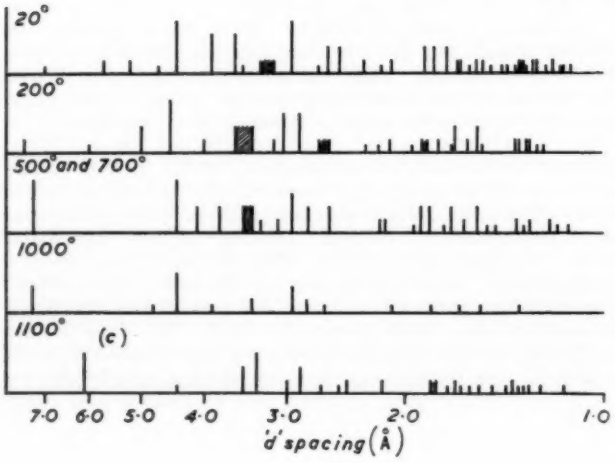

Fig. 7: K-*chabazite.*

The progressive changes in *X*-ray powder photographs following these heat treatments are illustrated in Fig. 5 (Li-chabazite), Fig. 6 (Na-chabazite), Fig. 7 (K-chabazite), Fig. 8 (NH_4-chabazite), and Fig. 9 (Ca-chabazite). These studies confirm that in many cases the basic structure of the chabazites remains unchanged both during, and for an interval after, water loss.

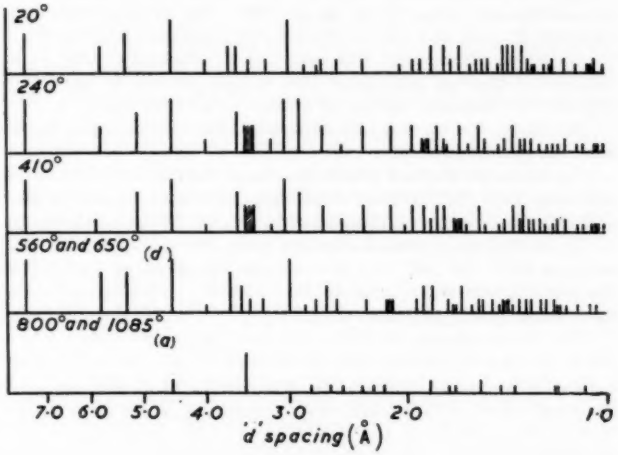

Fig. 8: NH_4-*chabazite.*

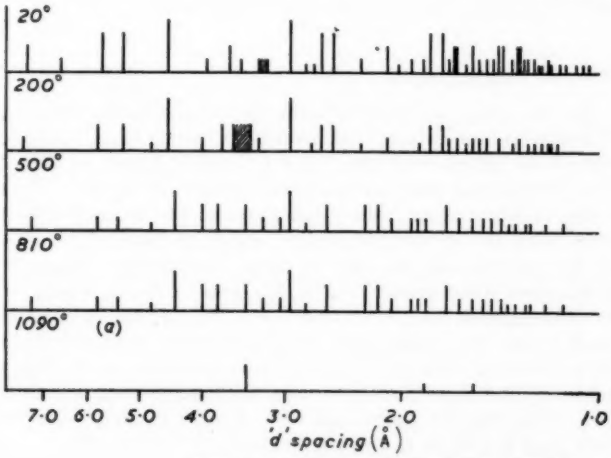

Fig. 9: Ca-*chabazite.*

FIGS. 5—9. *Lattice alterations with increasing temperature.*
a, Quartz. *b*, β-Eucryptite. *c*, Leucite. *d*, H-chabazite.

The patterns obtained for samples of Li-chabazite heated to 200°, 400°, and 600° are almost exactly identical, showing little evidence of alteration during dehydration of the crystals. After the first exotherm of this material (Fig. 1), *i.e.*, for the sample heated to 850°, the lattice was completely destroyed, and a weak quartz pattern appeared. After the second exotherm a strong β-eucryptite pattern was obtained.

The patterns of Na-chabazite heated to 200°, 400°, and 600° are identical in the low-angle diffractions but, between 200° and 400° where most of the water is lost, displacements of some of the weaker medium- and high-angle lines are observed. The 600° pattern is retained up to the temperature of the exothermic peak of the thermogram (Fig. 1), but by 1070° there is only a weak quartz pattern.

XUM

The *X*-ray powder photographs of specimens of K-chabazite, heated to various temperatures, show the same trend. The diffraction photograph for the 200° sample shows appreciable differences from that of the untreated sample, even among the strong lines at the low-angle end of the film. These shifts correspond to a small lattice contraction. Between 500° and 700° no reaction occurred, but at 1000° considerable lattice breakdown has taken place, while after the exothermic peak of Fig. 2, at 1090°, the product was amorphous. However, a further 12 hours' heating at 1100° resulted in recrystallisation to leucite.

Only one photograph was taken of Rb-chabazite, that of a sample heated to 1070° in a differential thermal analysis. This sample proved to have the same powder pattern as the original Rb-chabazite except for a weakening of the lines.

Similarly, the Cs-rich chabazite of Table 1 after being heated to 1060° remained identical with the parent structure.

Ca-chabazite showed much the same thermal stability as the potassium form. Between 200° and 500° the medium- and high-angle lines showed some displacement. Between 500° and 810° there was no further change, but at 1090° a weak quartz pattern appeared.

In Sr-chabazite similar changes were observed. Up to 300° there was little alteration; between 300° and 500° changes in some line positions and intensities were noted, but at 700° the pattern was still similar to that at 300°. Photographs of samples heated above 900° all gave weak quartz patterns.

The *X*-ray results for NH_4-chabazite are rather difficult to understand. Already at 240° there are some significant differences from the pattern of the original unheated crystals. There is then little change between 240° and 410°; but at 560° and at 650° (*i.e.*, at temperatures just before and just after the first exotherm in Fig. 2) the *same* pattern was found, which was close to that of a sample of H-chabazite previously prepared and *X*-rayed in these laboratories.[13] A sample heated to 800° or above showed a weak quartz pattern only, so that evidently reactions occurring between 560° and 650° are superseded by complete lattice breakdown.

Discussion

The stability of the Li-, Na-, K-, Rb-, and Cs-rich forms of the chabazite shows an interesting gradation. Fig. 5 indicates how lattice breakdown is postponed to increasingly higher temperatures as the size of the cations increases. The Rb and Cs forms are indeed stable under the conditions of differential thermal analysis to 1000° or higher. This behaviour can be related to the capacity of the ions to fill space in the intracrystalline cavities in the chabazite lattice after the removal of zeolitic water by heat. The same behaviour has been observed with the Na, K, Rb, and Cs forms of analcite. While the Na form undergoes lattice breakdown when heated, the K, Rb, and Cs forms, which are anhydrous, remain stable to temperatures far above 1000°.[1,14] The smaller cavities in this zeolite are evidently filled by K (in leucite), Rb, and Cs without need for water molecules to saturate the intracrystalline volume. Such a degree of filling of the larger cavities in chabazite is not achieved, and there is room for additional water even when the lattice is very rich in cæsium. This may be the reason why, though cæsium evidently stabilises chabazite, it probably does not do so to the same extent as with analcite.

Consideration of the endotherms and corresponding weight-loss curves of differential thermal analysis has shown that sometimes (*e.g.*, for Li-, Sr-, and Ba-chabazite) the water is given up in more than one stage. This may be analogous to the situation described by Peng [9] for some fibrous zeolites. Peng considered that such stages indicated that water molecules in the zeolites are arranged in groups having different volatilities. However, there are other explanations. In the fibrous zeolites, where lattice rearrangements can occur rather easily on heating,[5] such rearrangements of themselves may change the environment of the water molecules remaining, and this in turn may alter the volatility of the remaining water. In the chabazite crystals which we have studied, the alumino-silicate framework is more robust and less prone to alteration than are those of the fibrous

[13] Barrer and Sammon, *J.*, 1955, 2838.
[14] Barrer, Baynham, and McCallum, *J.*, 1953, 4035.

zeolites. The cations, however, are just as mobile, and are closely associated with intracrystalline water. When the amount of this water falls sufficiently, the positions of some or all of the cations may be rearranged, thus changing the water volatility.

One other feature of the endotherms and thermogravimetric curves may be indicated. The larger the cation in a series such as Li, Na, K, Rb, Cs, the lower tends to be the temperature at which substantially all the water is lost. This suggests a retentivity for water which is readily explained in terms of the association between cations and water dipoles. The binding energy from this source should be smaller for bigger ions. The bivalent ions, again as expected, show a greater retentivity than do univalent ions of comparable radius (Ca > Na and Ba > K).

The chabazites used in the present study are rather siliceous. Because of this it is not surprising that a common product of sintering was quartz, which was formed from Li-, Na-, NH_4-, Ca-, and Sr-chabazite. Other species produced were β-eucryptite (from Li-chabazite), leucite (from K-chabazite), and H-chabazite (from NH_4-chabazite). From the known compositions of these phases it is seen that disproportionation normally accompanies decomposition by sintering. Thus, for quartz formation:

$$(M_2,M)O,Al_2O_3,5SiO_2 \longrightarrow \underset{\text{(glass)}}{(M_2,M)O,Al_2O_3,(5-n)SiO_2} + \underset{\text{(quartz)}}{nSiO_2}$$

The other disproportionation product is represented in this equation as a glass, since no other diffraction pattern accompanied the appearance of the quartz lines. If the glass is the usual network structure with aluminium and silicon in tetrahedral co-ordination, n in the reaction equation should not exceed about three, if the validity of Lowenstein's rule is accepted.

This and the two following papers form part of a programme of research on the physical chemistry of silicates, supported by the Nuffield Foundation, and one of us (D. A. L.) acknowledges the award of a scholarship from the Nuffield Foundation.

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777. *Reactions and Stability of Chabazite-like Phases. Part II.*[1] *Ion-exchanged Forms of Some Synthetic Species.*

By R. M. BARRER and D. A. LANGLEY.

Thermal stability of cation-exchanged forms of a natural siliceous chabazite and of a range of synthetic chabazite-like phases tends to decrease the more aluminous the phases. There appears to be a family of at least four natural and synthetic zeolites of chabazite type.

When minerals or phases produced from the cation-exchanged forms were based on aluminosilicate frameworks of different type from chabazite, mineral growth was normally preceded by a structural breakdown to an amorphous or glassy phase. In other cases the chabazite lattice changed directly into the lattice of the new species.

IN the preceding paper we traced the rather regular influences of cation on the thermal stability and reactions of various cation-exchanged forms of chabazite with a constant $SiO_2 : Al_2O_3$ ratio of 1 : 5·05. In the present paper we investigate, for a more limited series of cation forms, how systematic variations in the alumina : silica ratio influence the sintering reactions and stability of chabazite-like phases.

[1] Part I, preceding paper.

Experimental

The methods of differential thermal analysis, thermogravimetry, and *X*-ray diffraction employed in Part I have also been used here, supplemented by ion-exchange and analytical data (methods previously discussed). The compositions of the phases investigated are given in Table 1. From these crystalline powders Li-, Na-, and Ca-rich cation-exchanged forms were

Table 1. *Synthetic phases structurally related to chabazite.*[2]

	Molar proportions			
Specimen	K_2O	Al_2O_3	SiO_2	H_2O
K-G1	1·03	1·00	4·15	4·51
K-G2	0·95	1·00	2·72	4·65
K-G3	0·99	1·00	2·65	3·75
K-G4	1·11	1·00	2·56	3·48
K-G5	0·92	1·00	2·30	3·65

also prepared, by two treatments with saturated aqueous chloride solutions, which ensure virtually complete exchange.[3,4] This treatment was followed by hydrothermal extraction with water, washing several times with acetone, and air-drying. All the products were equilibrated over saturated calcium nitrate solution. The water contents recorded in Table 1 refer to material treated in this way, so they do not necessarily represent the water contents of the crystals originally prepared.[2]

Results

In Figs. 1—4 are shown the thermograms for the Li, Na, K, and Ca forms of each of the five phases of Table 1, and of the natural siliceous chabazite of Part I. With the successive curves is given the appropriate alumina : silica ratio for each experimental specimen. In every one of these diagrams there is a marked difference between the high-temperature end of the thermograms for the siliceous natural chabazite and the most siliceous of the synthetic chabazite-type phases. Moreover the aluminous phases also show some striking differences from either of the most siliceous phases, natural or synthetic.

The thermogravimetric curves for the Li, Na, and Ca forms of the six phases are shown in Figs. 5—7. In addition these curves were determined for most of the K-rich forms, but these all gave very smooth and similar curves, the water being completely lost by 400°. This similarity among the K-rich phases extends also in the lower-temperature range to the differential thermal analyses shown in Fig. 3. The endothermic sections of these curves all show a small sub-peak, towards the end of the region of water loss. In K-chabazite this sub-peak occurs at 325°, while in the synthetic phases it occurs at about 260—280°.

The differential thermal analysis curves of the Na forms (Fig. 2) resemble more closely those of the Ca-rich phases (Fig. 4) than those of the K phases shown in Fig. 3, except in the case of Na-G1. In the aluminous phases sub-peaks in the endotherms for water loss are strongly developed. The similarity between Na-G4 and Ca-G4 in this region is very marked. The thermogravimetric curves of the aluminous forms (Fig. 6) show some rather sharp changes in slope which suggest that the sub-peaks in the endotherms are associated with sudden releases of water.

The differential thermal analyses of the Li forms (Fig. 1) also show similarities with both the Na and the Ca phases, rather than with the K phases. The sub-peaks are often well developed, and are reflected in rather sudden changes in slope in the thermogravimetric curves (Fig. 5). Thus, as in the cases of the Na and the Ca phases (Figs. 6 and 7) these sub-peaks must also refer to sudden releases of water.

The differential thermal analyses of the Ca phases (Fig. 4) are in some respects the most complex which were observed. The endothermic region of the curve for Ca-chabazite continues to nearly 800° and is associated with some weight loss even above 700°, as shown by the uppermost thermogravimetric curve of Fig. 7. In the thermograms of Ca-G2 and Ca-G5 the normal endothermic section associated with water loss at lower temperatures comprises a doublet

[2] Barrer and Baynham, *J.*, 1956, 2882.
[3] *Idem*, *J.*, 1956, 2892.
[4] Barrer and Sammon, *J.*, 1955, 2838.

FIG. 1.

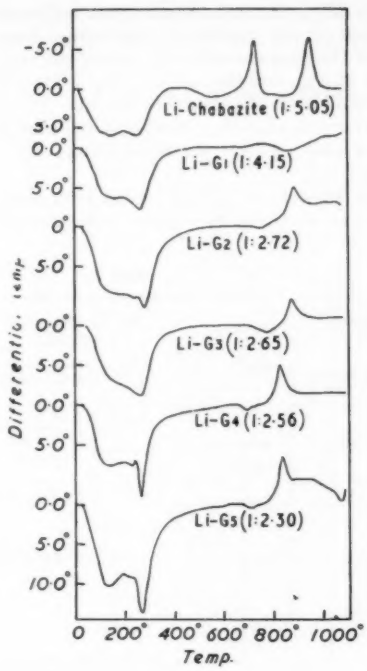


FIG. 2.

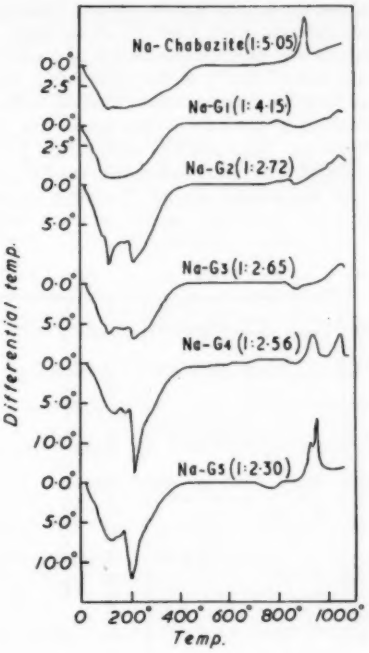


FIG. 3.

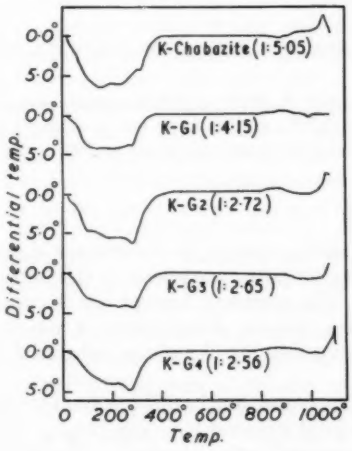
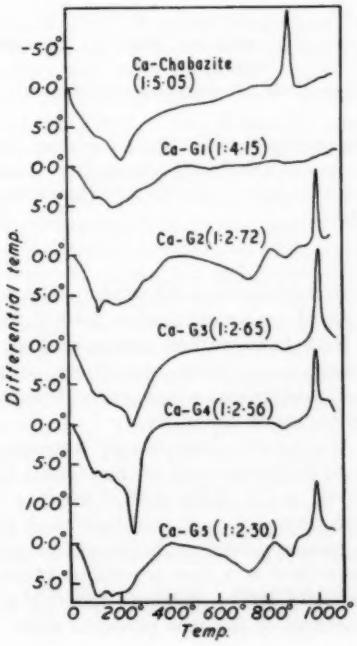


FIG. 4.



FIGS. 1—4. *Thermograms of* (*Fig.* 1) Li *phases*, (*Fig.* 2) Na *phases*, (*Fig.* 3) K *phases*, (Fig. 4) Ca *phases*.

extending from room temperature to about 420°. It is succeeded by additional endothermic regions, the first of which extends from about 430° to 830°. Then a second small, rather sharp peak extends from 830° to about 930°. Comparison of the curves for differential thermal analysis and thermogravimetry of Ca-G2 shows that the first endothermic region corresponds to the loss of 72·8% of the total water, the second to 25·5%, and the last to 1·7%. Thus there may be three types of water binding in this sample, and also in the specimen Ca-G5. From the viewpoint of the exothermal peaks the differential thermal analysis curves also fall into three categories. Ca-chabazite shows this peak at about 860°; Ca-G1 shows no peak; and the remaining four phases all show a similar peak at 1000°.

All the phases, for which curves are presented in Figs. 1—4, were *X*-rayed after separate specimens had been heated to each of a sequence of successively higher temperatures, as

FIG. 5.

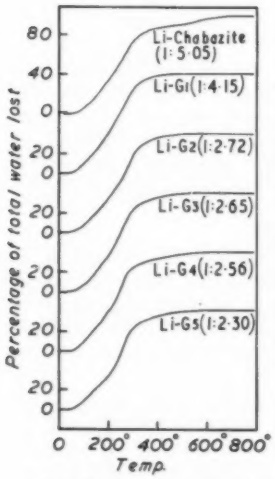


FIG. 6.

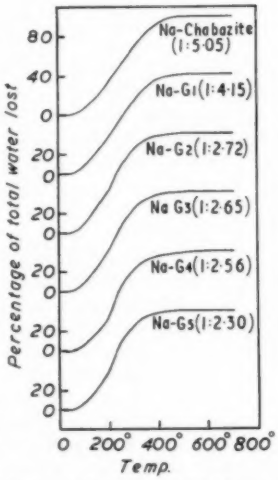
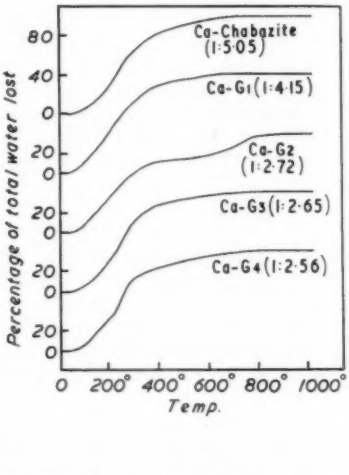


FIG. 7.



FIGS. 5—7. *Thermogravimetric curves for* (*Fig.* 5) Li *phases,* (*Fig.* 6) Na *phases,* (*Fig.* 7) Ca *phases.*

indicated in Part I. The Ca-zeolites, after being heated at 1090°, yielded felspars similar to, but not identical with, anorthite. This is preceded by formation of a glassy phase already present at 940°. On the other hand (Part I) the natural siliceous chabazite at 1090° produced quartz.

DISCUSSION

Recrystallisation Reactions.—The products of heat-treatment in the manner described in Part I are summarised in Table 2, for four of the chabazite-type phases of this paper and of Part I, in various cation-exchanged forms. The products formed are surprisingly numerous, including amorphous or glassy phases, quartz, β-eucryptite, a nosean-like phase, nepheline, α-carnegieite, leucite, kaliophilite, a hauyne-like phase, calcium felspar, and hydrogen chabazite.

Quartz was obtained only from the most siliceous phase, but in this one instance it was obtained from several of the cationic forms. The most siliceous K phases ($Al_2O_3 : SiO_2 =$ 1 : 5·05 and 1 : 4·15) yielded leucite as the only recrystallisation product. The two most aluminous phases, on the other hand, yielded only kaliophilite, and the two most aluminous Na phases yielded nepheline as final product. In the large majority of these reactions the appearance of a new crystalline phase is preceded by a temperature range in which the chabazite lattice becomes amorphous or glassy. This is the course taken when the structures of the new products differ very much from that of chabazite. The products

often differ considerably in $Al_2O_3 : SiO_2$ ratio from the original phase, so that the crystallisations involve not only nucleation from the amorphous or glassy breakdown product of the chabazites but at the same time disproportionation.

TABLE 2. *Effects of heating upon chabazite-type phases.*

$Al_2O_3 : SiO_2$ ratio	Cation form	Products and heating temperatures
1 : 5·05	Li	Li-Ch * (200°) Li-Ch (400°) Li-Ch (600°) *quartz* (850°) *β-eucryptite* (1070°)
	Na	Na-Ch (200°) Na-Ch (400°) Na-Ch (600°) modified Ch (820°) *quartz* (1070°)
	K	Modified Ch (200°) modified Ch (500 and 700°) unidentified (1000°) *leucite* (1100°)
	NH_4	Modified Ch (240°) modified Ch (410°) H-*Ch* (560 and 650°) *quartz* (800 and 1095°)
	Ca	Ca-Ch (200°) Ca-Ch (500°) modified Ch (810°) *quartz* (1090°)
1 : 4·15	Li	Li-Ch (200°) modified Ch (550°) mainly glassy (820°) *β-eucryptite* (1070°)
	Na	Na-Ch (160°) Na-Ch (500°) Na-Ch (700°) *glassy* (920°) *glassy* (1070°)
	K	Modified Ch (200°) modified Ch (550°) modified Ch and *amorphous* (700°) *glassy* (970°)
	Ca	Ca-Ch (200°) modified Ch (500°) modified Ch (700°) *glassy* (940°) Ca-*felspar* (1090°) *leucite* (1100°)
1 : 2·65	Li	Modified Ch (200°) modified Ch and *amorphous* (550°) *glassy* (820°) *β-eucryptite* (1060°)
	Na	Na-Ch (160°) modified Ch and some *nosean* (500 and 700°) *nosean* (940°) *nepheline* (1080°)
	K	Modified Ch (200°) modified Ch and *amorphous* (500 and 700°) *glassy* (980°) *kaliophilite* (1080°)
	Ca	Ca-Ch (200°) modified Ch and some *hauyne* (550°) *glassy* (940°) Ca-*felspar* (1090°)
1 : 2·30	Li	Li-Ch (200°) *amorphous* (550°) *β-eucryptite* (900 and 1080°)
	Na	Na-Ch (170°) *nosean* (300°, 500°, and 840°) *α-carnegieite* (950°) *nepheline* (1080°)
	K	Modified Ch (200°) *largely amorphous* (500°) *glassy* (700 and 950°) *kaliophilite* (1090°)
	Ca	Modified Ch (200°) *hauyne* (500°, and 820°) *glassy* (900°) Ca-*felspar* (1080°)

* Ch denotes parent chabazite-like phase.

There are exceptions. First are minor changes in line intensity and position associated with heating and water loss, in which the chabazite-type of structure is preserved in a slightly modified form. These changes may involve, not only water loss, but also rearrangement of cations and small adjustments of the anionic framework. The " modified chabazites " and hydrogen chabazite of Table 2 are of this kind. There is another somewhat more extensive change which also does not involve the preliminary transformation into a glassy phase. This is the change from structures related to chabazite to structures like those of nosean–hauyne minerals. The change in this case involves alteration in crystal symmetry from rhombic to cubic. Nosean felspathoids and chabazite zeolites were thought to be based on the same arrangement of polyhedra in 8-fold co-ordination.[5] Each polyhedron of the former is, or approximates to, a regular cubo-octahedron built from $(Al,Si)O_4$ tetrahedra, and has six faces circumscribed by rings of four tetrahedra and eight faces circumscribed by six-membered rings. But a new structure, different from that of the nosean–sodalite felspathoids, has been suggested [5a] for chabazite, thus making the observed transformation of interest. The transformation of chabazites at low temperatures into nosean-type structures has been noted previously in this laboratory:[3] it is confined to the more aluminous chabazite-type phases. This appears to reflect the limitation in composition of the nosean–sodalite felspathoids where the ratio $Al_2O_3 : SiO_2$ is close to the value 1 : 2. Thus for a siliceous chabazite to be converted without disproportionation into a nosean felspathoid would require a gross departure from the alumina : silica ratio characteristic of these felspathoids. A novel feature of the nosean- and hauyne-like structures formed in the present work is that there cannot be any of the

[5] Pauling, *Proc. Nat. Acad. Sci.*, 1930, **16**, 453; *Z. Krist.*, 1930, **74**, 213; Bragg, " Atomic Structure of Minerals," Oxford Univ. Press, 1937, p. 265; Wyart, *Bull. Soc. franç. Mineralog.*, 1933, **56**, 81.
[5a] Dent and Smith, *Nature*, 1958, **181**, 1794.

included species (NaOH, Na_2CO_3, NaCl, Na_2SO_4, $CaCO_3$, etc.) which are normally present within cavities in other natural and synthetic felspathoids.

The products of reaction from chabazite include four species which Buerger [6] has termed " stuffed " derivatives of crystalline silica. Thus eucryptite [7] is based on a high-quartz structure in which $Al^{3+} + Li^+$ replace half of the Si^{4+} atoms of the framework. The Li^+ ions are present in interstices in this anionic framework. Eucryptite was obtained from every Li-chabazite phase whatever the $Al_2O_3 : SiO_2$ ratio. Nepheline is another stuffed derivative based this time on a tridymite structure slightly collapsed by a distortion of the framework. Kaliophilite is also regarded as a stuffed derivative of tridymite although its detailed structure is not known. Finally, α-carnegieite [8] is a stuffed derivative of cristobalite. Both carnegieite and nepheline are different forms of $NaAlSiO_4$, nepheline being the stable form below 1248°.[9] Thus the α-carnegieite obtained in this work has appeared in a range of temperature in which it is metastable.

Stability of Chabazite-type Phases.—We have now examined the stability to heat of chabazite-like phases covering a wide range in alumina : silica ratios and for a series of cation-exchanged forms of each phase. For any given cation-exchanged form loss of crystallinity or recrystallisation of the parent phase occurs at a lower temperature the more aluminous the phase becomes. In a zeolite structure, in which the ratio base : alumina is always 1 : 1, the more aluminous the mineral the greater are its framework charge, cation density, and cation-exchange capacity. It may then be this high framework charge which modifies the stability of the aluminous minerals. A number of other variations in properties have been traced in relation to changing $Al_2O_3 : SiO_2$ ratios for these chabazite-type phases.[2,3]

In Part I [1] we have shown that for a series of ion-exchanged forms the thermal stability of a siliceous natural chabazite increases in the sequence $Li < Na < K < Rb < Cs$. The situation among the more aluminous phases for the more restricted series of ions Li^+, Na^+, and K^+ is less well defined. However, the Na and K forms are of comparable stability. The Ca form also, among the siliceous phases, is of considerable stability.

Classification of Chabazite-type Phases.—Earlier investigations,[2,3] and especially those in Part I and in the present paper, provide evidence that there are various members of what may be termed the chabazite family of zeolites. These members differ sufficiently from one another to be regarded as separate species, in the way in which chabazite and gmelinite are already so considered. Nevertheless there are similarities in the alumino-silicate frameworks.

As noted above, the curves in Figs. 1—4 are of three distinct types. The siliceous natural chabazite is well distinguished from the most siliceous synthetic phase, which is equally well distinguished from the remaining synthetic phases having $Al_2O_3 : SiO_2$ ratios from 1 : 2·72 to 1 : 2·30. There are also variations in *X*-ray diffraction patterns, gas-sorbing properties, and refractive indices which have in part been traced elsewhere.[2,3] Among the synthetic phases there is some evidence of a discontinuity between those with Al_2O_3/SiO_2 less than 3 and those in which this ratio exceeds 3.

On the basis of such studies we suggest the following classification of members of the chabazite family: (i) chabazite, (ii) gmelinite, (iii) synthetic K-species [2,3] with $Al_2O_3/SiO_2 > 3$, (iv) synthetic K-species [2,3] with $Al_2O_3/SiO_2 < 3$.

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IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, March 17th*, 1958; *Revised, July 23rd*, 1958.]

[6] Buerger, *Amer. Mineralog.*, 1954, **39**, 600.
[7] Winkler, *Acta Cryst.*, 1948, **1**, 27.
[8] Bowen and Greig, *Amer. J. Sci.*, 1925, **10**, 204.
[9] Barrer and Bultitude, unpublished work.

778. *Reactions and Stability of Chabazite-type Phases. Part III.* Intracrystalline Water.*

By R. M. Barrer and D. A. Langley.

The intracrystalline water in a series of non-stoicheiometric hydrates based on the chabazite lattice has been studied by differential thermal analysis, thermogravimetry, and *X*-ray powder photography applied to a variety of ion-exchanged forms and, in some cases, for a variety of $Al_2O_3 : SiO_2$ ratios, all equilibrated at a relative humidity of ~0·51.

In a natural chabazite the affinity for water decreased for a range of ion-exchanged forms in the sequence Ca > Li > Na > K, Rb > Cs. With increasing $Al_2O_3 : SiO_2$ ratio the actual water content per structural cage increased for Ca and Li forms. For all forms there was a tendency, despite some irregularities, for the number of water molecules per cation to decrease with increasing number of cations per cage, with increasing cation radius, and with decreasing primary hydration number of the solvated cations.

Integral heats associated with water loss have been determined for various forms of a natural chabazite and of chabazite-type phases of varying $Al_2O_3 : SiO_2$ ratios. These heats do not depend in a simple way on cation radius or on the number of cations per unit cell. It is suggested that cation positions may alter as cation radius changes and that some crystals undergo perturbations during water loss. Heats are influenced by ion-dipole interactions whose magnitude is however reduced in the intracrystalline environment.

Crystallohydrates may be stoicheiometric or non-stoicheiometric in water content. The zeolites comprise a diverse group of non-stoicheiometric hydrates, and the behaviour of their intracrystalline water has been studied in relation to diffusion,[1] dielectric relaxation,[2] infrared absorption,[3] optics,[4] crystallography,[5] sorption equilibria,[6,7] sorption heats,[7,8] and exchange of light and heavy water.[9] Nevertheless, the detailed properties of crystal water remain obscure in many respects.

As a result of studies of hydrothermal crystallisation of aluminosilicates it has been possible[10] to prepare a series of chabazite-type phases in which (*a*) the alumina : silica ratio varies over a wide range, (*b*) the cation density varies to correspond with this ratio, (*c*) the cations present may be exchanged, to vary the ion radius and valency, and (*d*) the water content can be varied continuously in the crystals of all exchange forms.

We now report a comparative study of the intracrystalline water in these phases, having used differential thermal analysis, thermogravimetry, and *X*-ray powder photography, as in Parts I and II.[11] It has been our principal interest to obtain comparative values of integral heats for water loss in relation to alumina : silica ratios and cation

* Parts I and II, preceding papers.

[1] Tiselius, *Z. physik. Chem.*, 1934, *A*, **169**, 425; 1935, *A*, **174**, 401; Barrer, "Diffusion in and through Solids," Cambridge Univ. Press, 1951, p. 97 *et seq.*

[2] Wetzlar, *Z. angew. Mineralog.*, 1938, **1**, 125; Cook and Meakins, *Trans. Faraday Soc.*, 1955, **51**, 1483.

[3] Pickett, *Amer. Mineralog.*, 1949, **34**, 861; Passerini, *Gazzetta*, 1935, **65**, 534.

[4] Rinne, *Neues Jahrbuch Mineralog.*, 1897, I, 41; II, 28; 1899, I, 1; Weigel, *Sitzungsber. Akad. Wiss. München, Math.-Phys. Klasse*, 5 Oct. 1919; Slawson, *Amer. Mineralog.*, 1925, **10**, 305.

[5] Taylor, *Proc. Roy. Soc.*, 1934, *A*, **145**, 80; Bragg, "Structure of Minerals," Cornell Univ. Press, New York, 1937, p. 262.

[6] Hey, *Mineralog. Mag.*, 1935, **24**, 99.

[7] Barrer, *Ann. Reports*, 1944, **41**, 31.

[8] Tiselius and Brohult, *Z. physik. Chem.*, 1934, *A*, **168**, 248.

[9] Kraft, *Z. Physik*, 1938, **110**, 303; Duhm, *Götting. Nach.*, 1936, **2**, 123; Faucher and Thomas, *J. Phys. Chem.*, 1955, **59**, 189.

[10] Barrer and Baynham, *J.*, 1956, (*a*) 2882, (*b*) 2892.

[11] Barrer and Langley, preceding papers.

type and radius. Various difficulties are associated with attempts to obtain quantitative heat data by differential thermal analysis, although suggestions have been made from various sources for improving the technique as a quantitative procedure.[12] It is however probable that useful comparative date will follow when a series of structurally very similar phases, all based on one aluminosilicate framework, is the subject of study, and if these phases remain structurally unaltered over the temperature interval required for water loss. These criteria are largely fulfilled by the crystals studied in this research.

Experimental

Materials.—The crystalline zeolites examined were those already described in Parts I and II, *i.e.*, they were cation-exchanged forms of a natural chabazite with an alumina : silica ratio of 1 : 5·05, and of synthetic chabazite-type phases where this ratio is 1 : 4·15 (species G1), 1 : 2·72 (G2), 1 : 2·65 (G3), 1 : 2·56 (G4), and 1 : 2·30 (G5). In addition, Linde molecular sieve 4A kindly supplied by Linde Air Products Co. Ltd. was examined.[13] This sieve is a synthetic zeolite: the composition [14] of the specimen used in this work can be represented as $Na_{12}[(AlO_2)_{12}(SiO_2)_{12}]NaAlO_2.27H_2O$, the water content being however rather variable.

Determination of Water Content.—The crystalline ion-exchanged forms of the chabazite-type phases were all brought into equilibrium with saturated calcium nitrate solution, by leaving

Table 1. *Weight losses (%) by ignition and by thermogravimetry.*

Sample	Ignition	Thermo-gravimetry	Sample	Ignition	Thermo-gravimetry
Li-chabazite	20·86	20·44	K-G4	15·66	14·84
Na-chabazite	19·06	18·76	Ca-G1	21·14	19·94
K-chabazite	15·66	15·16	Ca-G2	23·74	23·15
K-G1	15·91	15·35	Ca-G3	23·16	22·56
K-G2	19·59	19·10	Ca-G4	22·05	21·86
K-G3	16·76	16·01	Ca-chabazite	21·11	20·50

Table 2.

Sample	Total heat (cal.)	Area under curve (mm.²)	cal./10³ mm.²
$CuSO_4.5H_2O$	50·85	13,077	4·112 [a]
H_2O(l)	32·25	7,732	4·172
$CaSO_4.2H_2O$	13·76	3,445	3·996
$BaCl_2.2H_2O$	58·18	14,324	4·061 [b]
Mixture I	75·65	18,856	4·012
Mixture II	70·18	18,252	3·845

[a] Mean of three determinations. [b] Mean of two determinations.

them in desiccators containing the solution. Water contents were originally determined by ignition in platinum crucibles, over a Meker burner. However, weight losses by such ignition were all slightly, but significantly, greater than those obtained from thermogravimetric curves with temperatures rising to about 1100° (Table 1), probably owing to a small loss of alkali at 1250°; water contents were therefore determined from the thermogravimetric curves (Parts I and II).

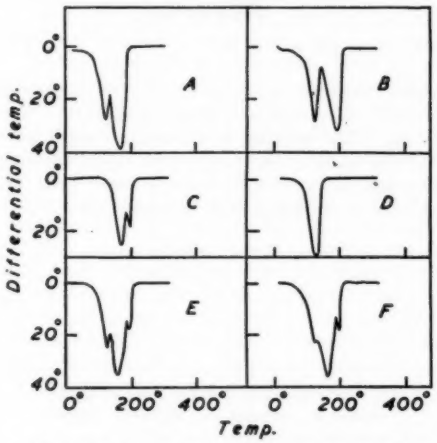
Standardisation of the Apparatus for Differential Thermal Analysis.—The apparatus for differential thermal analysis was calibrated as follows. Its accuracy for our purpose was first assessed. Several reactions (*A*—*D*) having known heats were employed for this purpose, also mixed reactions ($A + C$) with known amounts of each reactive component. The water in reaction *D* was dispersed in ignited kaolin powder. The powdered reactants were prepared and packed as described in Part I. The curves for the reactions used in calibration are shown in Fig. 1. The double endothermic peaks indicate a water loss in steps. Areas under these

[12] Wittels, *Amer. Mineralog.*, 1951, **36**, 615, 760; Eyraud, *Technica*, 1954, **177**, 2; Lodding and Sturm, *Amer. Mineralog.*, 1957, **42**, 78; Boersma, *J. Amer. Ceram. Soc.*, 1955, **38**, 281.
[13] Breck, Eversole, Milton, Reed, and Thomas, *J. Amer. Chem. Soc.*, 1956, **78**, 2338.
[14] Barrer and Meier, unpublished work.

(*A*) $CuSO_4,5H_2O \longrightarrow CuSO_4,3H_2O + 2H_2O(g)$	ΔH_{373}	$26{\cdot}4_9$	kcal./mole		
$\longrightarrow CuSO_4,H_2O + 4H_2O(g)$	ΔH_{388}	$27{\cdot}3_4$	,,		
$\longrightarrow CuSO_4 + 5H_2O(g)$	ΔH_{502}	$17{\cdot}3_4$	,,		
overall	ΔH	$71{\cdot}1_7$	,,		(ref. 15)
(*B*) $BaCl_2,2H_2O \longrightarrow BaCl_2,H_2O + H_2O(g)$	ΔH_{383}	$13{\cdot}1_4$	,,		
$\longrightarrow BaCl_2 + 2H_2O(g)$	ΔH_{425}	$14{\cdot}8_9$	,,		
overall	ΔH	$28{\cdot}0_3$	,,		(ref. 16)
(*C*) $CaSO_4,2H_2O \longrightarrow \alpha\text{-}CaSO_4,\frac{1}{2}H_2O + 1\frac{1}{2}H_2O(g)$	ΔH_{401}	19·52	,,		
$\longrightarrow \alpha\text{-}CaSO_4 + 2H_2O(g)$	ΔH_{436}	7·31	,,		
overall	ΔH	$26{\cdot}8_3$	,,		(ref. 17)
(*D*) $H_2O(l) \longrightarrow H_2O(g)$	ΔH_{373}	9·72	,,		(ref. 18)

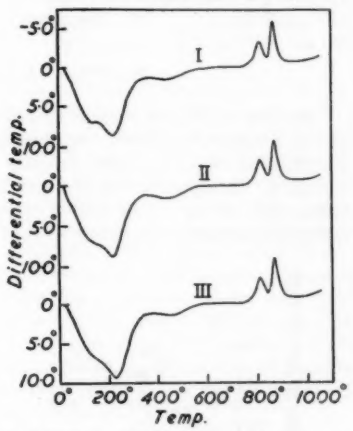
curves were evaluated graphically. If these areas are proportional to the heat of reaction we may hope to find the same constant of proportionality over the group of reactions, and can then extend the method to measure heats associated with water loss from the zeolites. The results, summarised in Table 2, show an average value of 4·06 cal. per 10^3 mm.^{2}, with maximum

FIG. 1. *Thermograms for hydrates whose heats of hydration are known.*



A, $CuSO_4,5H_2O$. *B*, $BaCl_2,2H_2O$. *C*, $CaSO_4,2H_2O$. *D*, H_2O. *E*, *Mixture I* (*A* + *C*). *F*, *Mixture II* (*A* + *C*).

FIG. 2. *Thermograms for Linde molecular sieve 4A* (Na *form*).



I, 0·2779 g. ($\Delta H = 18{\cdot}5_1$ *kcal. per mole of* H_2O).
II, 0·2868 g. ($\Delta H = 18{\cdot}4_6$ *kcal. per mole of* H_2O).
III, 0·2861 g. ($\Delta H = 18{\cdot}4_6$ *kcal. per mole of* H_2O).

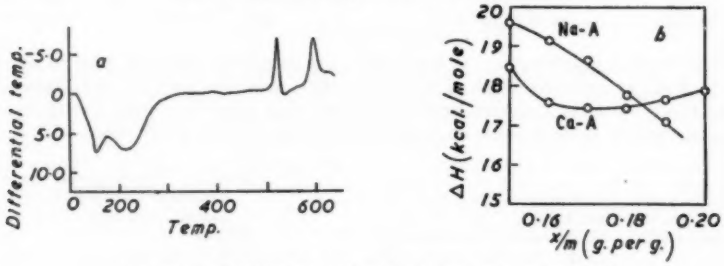
deviations of about −5·4 and +3·8%. Since the thermal conductivities of the several chemically distinct powders may differ appreciably this result is satisfactory. Probably most of the heat of reaction is removed *via* the gas and the vapour phase, rich in water vapour, and common to all reacting species.

Reproducibility of Heat Determinations.—The reproducibility of endotherms and integral heats associated with water loss was next investigated. The curves for differential thermal analysis of three samples of Linde molecular sieve 4A (Na form) are shown in Fig. 2. From the areas of the endotherms and the constant 4·06 cal. per 10^3 mm.^{2} integral heats of $18{\cdot}5_1$, $18{\cdot}4_6$, and $18{\cdot}4_6$ kcal./mole of water were obtained. The thermogram for the Ca form (sieve 5A) is shown in Fig. 3, and gives an integral heat of $17{\cdot}0_0$ kcal./mole of water removed. The

[15] International Critical Tables, 1926 Edn., Vol. VII, p. 263 (section on Free Energies).
[16] "Selected Values of Chemical Thermodynamic Properties," Nat. Bur. Stand., Washington, 1949, Series I, Vol. I, Table 87—5.
[17] *Op. cit.*, Tables 89—2, 89—3, 89—4.
[18] Ref. 15, p. 232; also Richards and Matthews, *Proc. Amer. Acad. Arts Sci.*, 1911, **46**, 511; Smith, *Phys. Rev.*, 1911, **33**, 173.

figure also reproduces the *differential* heats obtained from sorption data, as a function of amounts sorbed ranging from 0·5 up to 0·62 and 0·67 of saturation, by Breck *et al.*[13] Integral heats between these limits can be found by graphical integrations from this value and are of the same order as our integral heats, although the different ranges in amounts sorbed preclude any close comparison. Still more satisfactory, however, is the agreement between the three integral heats determined from the endotherms of Fig. 2.

FIG. 3. *(a) Thermogram for Linde molecular sieve 5A* (Ca *form) leading to integral heat. (b) Differential heat as a function of amount sorbed (ref.* 13).



(a) refers to 0·2875 *g.*; $\Delta H = 17{\cdot}0_0$ *kcal. per mole of* H_2O.

Stability of Phases to Heating and Cooling Cycles.—Natural chabazite was heated in the cell of the differential thermal analysis apparatus to ~600°, then cooled to room temperature, and equilibrated over saturated calcium nitrate solution. The heating and cooling cycles were repeated. Samples of the Na and the K form of the natural chabazite were taken through three such cycles. The curves were reproducible and *X*-ray examination showed that the materials remained unaltered, so that these natural chabazite phases show considerable stability

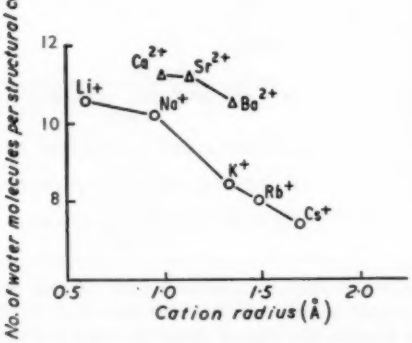


FIG. 4. *Variation of water content of natural chabazite enriched in different cations, with cation radius.*

under conditions obtaining during dehydration in the cell. *X*-Ray results reported in Part II show that the aluminous chabazite-type phases are sometimes less stable than the siliceous forms.

Water Content and Cation Type and Density.—Some equilibrium water contents at a relative humidity of ~0·51 are given in Table 3. The chabazite structure contains large cavities, each able to hold a cluster of water molecules.[19,20] The Table shows the average number of water molecules per cage. The cluster size (in terms of number of molecules at $p/p_0 \sim 0{\cdot}51$) decreases as the cation size increases, although with several irregularities, and also as cation valency decreases. The effect of cation size could indicate that larger cations occupy a significant fraction of the volume of the cages. However, cation size is clearly not the only factor involved

[19] Wyart, *Bull. Soc. franç. Mineralog.*, 1933, **56**, 106.
[20] Dent and Smith, *Nature*, 1958, **181**, 1794.

because, as the number of Ca and Li cations per cage increases, so also does the number of water molecules per cage. These two cationic forms of the zeolite contain the ions most likely to bind water energetically, and evidently the more of these ions in the cages the greater the water retentivity at $p/p_0 \sim 0{\cdot}51$.

TABLE 3. *Water molecules per structural cage at* $p/p_0 \sim 0{\cdot}51$.

$Al_2O_3 : SiO_2$ ratio	Univalent cations per cage [10]	Ca form	Li form	Na form	K form
1 : 5·05	3·44	11·24	10·56	10·20	8·44
1 : 4·15	4·02	11·02	9·40	10·58	8·80
1 : 2·72	4·84	13·54	11·44	10·94	11·82
1 : 2·65	5·10	13·22	11·36	10·48	9·68
1 : 2·56	5·84	12·96	12·02	11·36	9·18
1 : 2·30	5·14	13·48	12·12	9·78	9·54

For the natural chabazite having an $Al_2O_3 : SiO_2$ ratio of 1 : 5·05 a more extensive series of cation forms was investigated. A correlation then appeared between water retentivity at $p/p_0 \sim 0{\cdot}51$ and cation radius, as indicated in Fig. 4. In this Figure the results for Ca, Sr, and Ba forms fall on an upper curve and those for the univalent ions Li, Na, K, Rb, and Cs on another. Reference to Table 1, Part I, shows that in all cationic forms exchange was virtually complete save in the following instances: Sr (79% exchange); Ba (90%); Cs (89·7%). In the first two of the preceding three ion-exchanged chabazites the residual ion was Na^+; in the third it was Ca^{2+}.

From Table 3 we may calculate, per Avogadro number of cubo-octahedral cages in chabazite, the total volume of cations plus water molecules contained in them at a relative pressure of $\sim 0{\cdot}51$. To the nearest whole number we then have, assuming a molecular volume of 18 cm.^{3} for water: Ca form 208; Li form 194; Na form 192; K form 172; Rb form 172; Cs form 168 cm.^{3} This volume varies with cation size, more than could reasonably be attributed to deviations of the molecular volume of intracrystalline water from its normal value. Thus, the cages in the Ca form are probably nearly saturated, at $p/p_0 \sim 0{\cdot}51$, but this is not true of the other forms. These results show the different intrinsic water retentivities of the various cation forms.

The intracrystalline environment of the cations necessarily restricts the extent of cation solvation. Nevertheless there is a general correlation between the numbers of water molecules per cation in natural chabazites and primary hydration numbers of the same cations in aqueous solution,[21] as shown in Table 4. Because of the restricted environment of the intracrystalline cations we should also expect to find fewer water molecules per cation as the number of cations increases, so that the aluminous chabazite-type crystals should contain less highly hydrated cations. Despite certain irregularities this is confirmed by the data in Table 5.

TABLE 4.

	Ca^{2+}	Li^+	Na^+	K^+	Rb^+	Cs^+
H_2O mols. per cation in natural chabazite ...	6·5	3·1	3·0	2·5	2·3	2·0 *
Primary hydration nos. of cations	6—8	6	5	3	2	—

* Calc. for the homoionic Cs form.

TABLE 5.

$Al_2O_3 : SiO_2$ ratios in crystals	Water mols. per cation			
	Ca form	Li form	Na form	K form
1 : 5·05	6·5	3·1	3·0	2·5
1 : 4·15	5·5	2·3	2·6	2·2
1 : 2·72	5·6	2·4	2·3	2·4
1 : 2·65	5·2	2·2	2·1	1·9
1 : 2·56	4·4	2·1	1·9	1·6
1 : 2·30	5·2	2·4	1·9	1·9

Heats Associated with Water Loss in Natural Chabazites.—We may assume, from the results in Table 2 and from the reproducibility of the endotherms for Linde molecular sieve 4A, that the areas of the endotherms for the various chabazite-type phases are proportional to the resultant of the heat terms for all processes occurring during removal of water from the crystals.

[21] Bockris and Conway, "Modern Aspects of Electrochemistry," Butterworths, London, Chapter 2.

We may also assume that the constant of proportionality obtained from the reactions of Table 2 (4·06 cal. per 10^3 mm.^{2}) is nearly the same for all the water desorption reactions, especially since the phases studied are based on the same structure. The resultant heats associated with water will be integral heats, and will be mean values over a considerable temperature interval, weighted towards the temperatures of maximum rate of water loss.

In Parts I and II the differential thermal analysis endotherms and corresponding thermogravimetric curves were presented for typical instances and discussed qualitatively. From the endotherms the areas enclosed with the base-line were evaluated and heats associated with water loss derived. These heats can be considered in different ways, of interest from different points of view. The results are given in Table 6. In the Cs-, Sr-, and Ba-rich form there were other cations present in smaller amount; and estimates, of which the following is typical, were made of heats for the homoionic forms.

The Sr-rich form is 79% exchanged and there is the equivalent of 3·44 univalent cations per cage, with 11·18 water molecules. The heat associated with water loss from a structural cavity was found from the endotherm of Part I to be 171·8 kcal./Avogadro no. of cavities. In the 79% Sr-form there are 1·36 Sr^{2+} and 0·72 Na^+ ion per cavity. In a homoionic Na form there are 3·0 water molecules per ion. As an approximation therefore we assume that there are $10·2 \times 0·72/3·44 = 2·14$ water molecules associated with Na^+ in the heteroionic crystal. The removal of these 2·14 molecules requires 30·6 kcal., so that 141·2 kcal. were involved in the loss of the remaining 9·04 water molecules, associated with 1·36 Sr^{2+} ions. This gives 15·6 kcal. per mole of water, a ratio of 6·6 molecules of water per Sr^{2+} ion, and the other heats of Table 6 for the homoionic Sr-form. Similar calculations gave for the homoionic Cs and Ba forms 2·0 and 6·1 water molecules per cation, and the heats of Table 6.

The thermogravimetric data (Part I) for Ca, Sr, and Ba forms of chabazite indicate that water losses are 99·1% and 99·6% complete respectively, at temperatures approaching 800°. The endotherms of the Li and the Ba form are complex and rather similar, and probably indicate that water loss is associated with other changes, such as re-arrangement of cations (Part I). Perturbations of the crystal of this type could modify heat changes associated with water loss, as may also minor alterations of the aluminosilicate framework. One therefore refers to heats associated with water loss rather than to heats of dehydration.

Despite possible thermal effects of crystal perturbations during water loss it is of interest to compare overall heats associated with water loss and heats of solvation of anhydrous ions by water in bulk (columns 3 and 5 of Table 6). The intracrystalline environment of the cations restricts their solvation (Table 4), but also they are probably partially shielded by the negative charge mosaic of the aluminosilicates. On both counts heats associated with water removal per g.-ion are reduced more than ion solvation in bulk water. Indeed, since a substantial part

TABLE 6.

Cationic form	Heat: kcal./mole of H_2O	Heat: kcal./g.-ion	Heat: kcal./A. no. of cavities	Heat of solvation of cation [22] (kcal./g.-ion)
Li	12·7	39·0	134	136
Na	14·3	42·4	146	114
K	14·9	36·6	126	94
Rb	13·3	30·8	106	87
Cs(0·897)Ca(0·103)	13·7 *	27·4 *	94·$_6$ *	80
Ca	20·3	134·2	230	410
Sr(0·79)Na(0·21)	15·6 *	103·8 *	178 *	376
	16·0 *†	108·3 *†	186 *†	—
Ba(0·90)Na(0·10)	22·3 *	135·6 *	233 *	346
	20·9 *‡	129·3 *‡	222 *‡	—

* Calc. for homoionic Cs, Sr, and Ba forms. † For first 98·19% of water loss, reached at 700°.
‡ For first 94·72% of water loss, reached at 550°.

of the heat associated with water loss may arise from interaction of water molecules with the anionic framework, cation–water dipole interactions within the crystal are probably small compared with ion–water molecule interactions in bulk water.

The heats associated with dehydration of a cavity (column 4, Table 6) are of particular interest because they approximate to heats required to vaporise the cluster of water molecules

[22] Bernal and Fowler, *J. Chem. Phys.*, 1933, **1**, 515.

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in the cavity. These clusters (cf. Table 3) range in size from 13·54 molecules for one of the Ca forms to 6·8 molecules estimated for the homoionic Cs form. In column 2 of Table 6 are given heats associated with water loss per mole of water removed. Heats for the Na, K, Rb, and Ca forms are particularly interesting because for these phases there is no evidence of important lattice perturbation during water loss, and no assumption is involved in calculation, these forms being homoionic.

TABLE 7. *Heats associated with water loss* (ΔH_1 = *kcal. per mole of* H_2O; ΔH_2 = *kcal./g.-ion*).

$Al_2O_3 : SiO_2$ ratio	ΔH_1				ΔH_2			
	Li form	Na form	K form	Ca form	Li form	Na form	K form	Ca form
1 : 5·05	12·7	14·3	14·9	20·3	39·0	42·4	36·6	134·2
1 : 4·15	21·7	21·5	17·9	18·0	52·6	56·7	39·1	98·5
1 : 2·72	23·3	24·3	17·6	22·1	55·0	54·8	43·0	123·4
1 : 2·65	19·0	16·6	16·0	22·0	42·3	35·0	30·4	114·2
1 : 2·56	24·2	21·6	14·7	23·9	49·7	42·0	23·1	106·1
1 : 2·30	25·9	21·2	—	21·7	61·0	40·3	—	114·0

Heats Associated with Water Loss in Relation to $Al_2O_3 : SiO_2$ *Ratios.*—The more aluminous a chabazite-type phase the greater the density of negative charges on the aluminosilicate framework and of the cations needed for electrical neutrality. This could modify the binding energy of intracrystalline water. Heats for Li, Na, K, and Ca forms of a series of chabazite-type phases of varying $Al_2O_3 : SiO_2$ ratios are shown in Table 7. For the synthetic phases rich in Li, Na, and Ca nearly all the heats ΔH_1 have higher values than for the corresponding forms in the natural chabazite having $Al_2O_3 : SiO_2 = 1 : 5{\cdot}05$. The heats for the K forms show some increases, but with a different trend. Higher heats may be due to the greater charge density in the more aluminous phases, but there are modifying factors, which may be related to lattice perturbations in some of the phases during water loss.

The heats ΔH_2 show other trends. ΔH_1 depends mainly upon the energy of bonding of water in the structure, but ΔH_2 depends on this energy and on the number of water molecules per cation. As the cation density increases the amount of water per cation, despite some irregularities, shows a tendency to decrease (Table 5). ΔH_2 is largest for the Ca-rich phases, and least for the K forms, as would be expected from considerations of ion valency and size, if electrostatic forces were important in binding the water. However, evidence has been presented above that ion-dipole energies are much reduced within the crystal, and indeed values of ΔH_1 for Ca are often not very different from those for other cationic forms (Table 7).

DISCUSSION

It is of particular interest to compare the binding energy of water molecules in liquid water with that of water molecules in clusters within the chabazite. To do this we must estimate the energy required to remove a group of water molecules from the liquid equal to the group of water molecules per cavity in the zeolite, without the collapse of the cavity in liquid water. We may estimate this energy as follows. The latent heat of vaporisation of water at 100° is $9{\cdot}7_2$ kcal./mole.[18] At this temperature the co-ordination number will be assumed to be either 6 or 8. The removal of the first water molecule (leaving a cavity equal in volume to the molecule) requires an energy of 19·44 kcal., and breaks either 6 or 8 bonds according to the co-ordination number. If the co-ordination number is 6, the next six water molecules removed each break 5 bonds and so may be considered to require 16·2 kcal./mole while the next 12 molecules removed each break 4 bonds and require 13 kcal./mole. If the co-ordination number is 8, the next eight molecules removed each break 7 bonds, requiring 17·0 kcal./mole, and the following 8 break 4 bonds each, for an energy of $9{\cdot}7_2$ kcal./mole. Thus, as the cluster removed increases in size the heat per mole of water falls from 19·44 towards lower values, eventually for large enough clusters approaching 9·72 kcal./mole.

For the actual cluster sizes found in the cages of the Ca, Li, Na, and K forms of the natural chabazites and in the synthetic more aluminous phases, the energies per mole of water needed to remove clusters of equal size from liquid water range from 16 to 15 kcal. (co-ordination number 6) or 17·3 to 15·5 kcal.(co-ordination number 8). While this

estimate and comparison are not rigorous, it is seen that the binding energy of water in the cages in chabazite for the K forms (Table 7) is not very different from that in liquid water. That in the Ca, Li, and Na forms is usually greater, by differing amounts—up to ~50% in the extreme instance (Li-G5). Ion–dipole interaction terms may contribute significantly here, although this interaction is evidently not the major part of the total energy of interaction, which must include dispersion, dipole–dipole, and dipole–induced dipole contributions. The oxygen framework of the zeolite may well simulate the oxygen structure of the liquid water, so that the method of comparison developed above may be reasonably adequate.

Factors associated with apparatus and technique which operate to reduce the accuracy of differential thermal analysis as a quantitative method are, on the evidence of Table 2 and Fig. 2, not dominant in the conditions existing in this work. Other physicochemical factors associated with the experimental materials are likely to contribute to some irregularities in sequences of heat values and of hydration: (1) Complete chemical analyses of the Li, Na, and Ca forms of the synthetic phases were not available; although the conditions of exchange were those known to effect very extensive exchange,[10] there could be a little potassium in some of these forms. (2) The phases are not all equally stable under the conditions of differential thermal analysis, and there is evidence from the thermograms of lattice perturbation in the range associated with water loss for some but not all the phases (Parts I and II). (3) The synthetic phases, although produced in good yield,[10] are not necessarily 100% pure.

The results in Table 7 in particular must be considered in the light of the above factors. Nevertheless it is thought that this paper gives a perspective of the influence of cation type and of varying number of cations per unit cell on water retentively and energy of bonding in chabazite-type phases. There are small differences in the water contents of the crystals as given in Table 3 and those in Table 3 of ref. 10*b*. This arises because the phases in the earlier work were not in contact with a solution of fixed relative pressure before water determination, but were equilibrated with the atmosphere under necessarily more variable conditions.

We are indebted to Mr. G. Bratt, B.Sc., of this Department, for independent measurements of the calibration data of Table 2.

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779. *Sorption by* NH_4^+- *and* Cs^+-*Montmorillonites, and Ion Fixation.*

By R. M. BARRER and J. S. S. REAY.

The sorptive capacities of samples of NH_4^+- and Cs^+-montmorillonites for N_2, O_2, A, CH_4, C_6H_6, and H_2O are related to the intersheet spacings of these clays which are intermediate between that for the natural clay and those of the alkylammonium derivatives previously studied.[1,2,3] Certain of the properties exhibited by the NH_4^+- and Cs^+-clays indicate fixation of these ions on dehydration of the clay, and several observations are made upon the factors controlling cation fixation.

PREVIOUS work here has shown that, whereas only polar sorbates such as water or methanol can penetrate between the sheets of dry Na^+-montmorillonite, many large polar and non-polar sorbates are freely intercalated by alkylammonium montmorillonites.[1-3] Two of the main factors controlling this penetration are the initial sheet

[1] Barrer and MacLeod, *Trans. Faraday Soc.*, 1954, **50**, 980.
[2] *Idem, ibid.*, 1955, **51**, 1290.
[3] Barrer and Reay, *ibid.*, 1957, **53**, 1253.

separation of the outgassed clay and the affinity of the sorbate for the interlamellar surfaces and ions. The alkylammonium clays previously studied have d_{001} spacings ranging from 13·95 Å for the Et_4N^+-clay to 12·0 Å for the $Me{\cdot}NH_3^+$-form as compared with 9·6 Å for the natural Na^+-clay. To estimate the importance of initial sheet separations intermediate between 9·6 Å and 12·0 Å we have now investigated sorption by NH_4^+- and Cs^+-montmorillonites.

Experimental

(1) X-*Ray and Isotherm Data.*—(a) *Materials.* The ion-exchanged derivatives were formed from the natural clay as previously described [1-3] by treatment with brines of the chloride of the required cation, washing free from excess of salt, and drying from alcohol, acetone, or ether. The purity of the gases used for sorption and the sorption techniques have also been mentioned elsewhere.[1-3]

(b) X-*Ray diffraction.* Cu-K_α radiation, and a flat plate camera 9—11 cm. from the specimen were used. On outgassing NH_4^+- and Cs^+-montmorillonites at 10^{-6} mm. Hg at

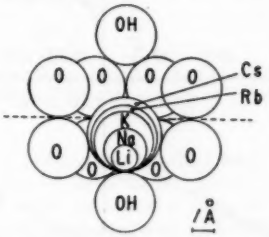

Fig. 1. *Cross-section of the cavity formed between two montmorillonite sheets in contact with one another showing the size of various cations in relation to the cavity.*

temperatures ranging from 25° to 160°, diffuse first-order lines and irrational series of 001 lines were obtained in the *X*-ray diffraction patterns. This is thought to be due to the ability of the dehydrated cations to sink appreciably into hexagonal holes in the sheet surface.

According to Hofman, Endell, and Wilm's structure,[4] these holes are 3·3 Å in "free diameter," a term denoting that diameter not occupied even by the periphery of the surrounding oxygen atoms. The radius of the oxygen atoms bordering the holes has been taken as 1·4 Å, as has that of the hydroxyl groups.[5] Fig. 1 shows that ions up to 2·4 Å in diameter could sink entirely below the sheet surface. Should the Cs^+ ion, sunk thus in a hole, be directly opposed on the adjacent sheet by a surface oxygen atom, the d_{001} spacing might be expected to be 10·6 Å. Whether Cs^+, of diameter 3·38 Å, would sink to the fullest extent is uncertain. With incomplete "burying" the maximum d_{001} spacing would be even greater than 10·6 Å. If holes on adjacent sheets are opposite one another it should be possible for the lattice to collapse to give a d_{001} spacing of 9·4—9·6 Å. In a turbostratic structure one may therefore expect an irrational series of lines in the *X*-ray diffraction pattern due to the variety of d_{001} spacings from 9·4 Å to >10·6 Å. A similar argument applies to the NH_4^+-clay.

The possibility also exists of the irrational series of lines being due to incomplete exchange by NH_4^+ and Cs^+. Estimation of nitrogen by the Kjeldahl method on a small sample of the NH_4^+-clay gave a content of 60—70 mequiv./100 g. as against 100 mequiv./100 g. of base exchange capacity of the original clay. The NH_4^+-clay was treated only with sodium hydroxide in the nitrogen estimation, and all the nitrogen may not have been released, especially as the clay had been outgassed and some of the NH_4^+ ions may have been fixed in the clay.

Attempted exchange of the Cs^+-clay back to the Na^+-form did not effect any change in the *X*-ray pattern. This again suggests fixation of Cs^+ in montmorillonite. This is not in opposition to the results of Faucher and Thomas,[6] who found a reversible ion-exchange isotherm for K–Cs–K exchange since their material was not outgassed in the Cs^+-form before the exchange back to the K^+-clay.

(c) *Sorption results.* Isotherms for oxygen, argon, nitrogen, and methane at 90° K are shown in Figs. 2 and 3. The sorption is considerable and the isotherms rise sharply up the

[4] Hofmann, Endell, and Wilm, *Z. Krist.*, 1933, **86**, 340.
[5] Barshad, *Proc. Amer. Soil Sci. Soc.*, 1952, **16**, 176.
[6] Faucher and Thomas, *J. Chem. Phys.*, 1954, **22**, 258.

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volume axis almost to the v_m value. The v_m values are intermediate between those for the natural clay, where sorption of these gases is limited to external surfaces of the crystallites, and those for organic derivatives such as $MeNH_3^+$- and Me_4N^+-clays where intercalation is known to occur [2,3] (Table 1).

The question arises whether intercalation of the permanent gases and of methane occurs in the NH_4^+- and Cs^+-clays. No expansion beyond that of the outgassed clay being assumed,

FIG. 2. *Isotherms for sorption by* NH_4^+*-montmorillonite.* N_2, CH_4, O_2, *and* A *at* 90° K, *and* C_6H_6 *at* 323° K.

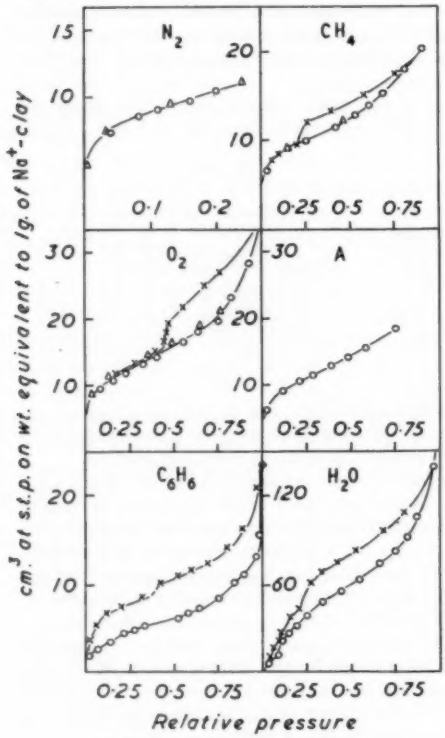

FIG. 3. *Isotherms for sorption by* Cs^+*-montmorillonite.* O_2, A, *and* N_2 *at* 90° K, *and* C_6H_6 *a* 323° K.

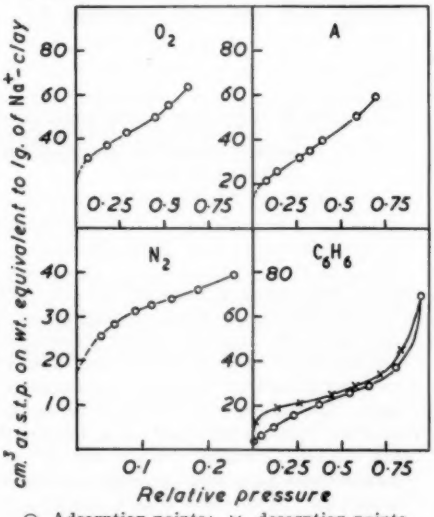

TABLE 1. *Sorption upon* NH_4^+ *and* Cs^+*-montmorillonites compared with the natural clay and the* $Me{\cdot}NH_3^+$*-form.*

		Clay							
		Natural		NH_4		Cs		$CH_3{\cdot}NH_3$	
Sorbate	T (°K)	v_m	A	v_m	A	v_m	A	v_m	A
N_2	90	4·95	21·68	8·92	40·6	30·9	141	43·4	198
O_2	90	5·74	21·88	9·82	37·0	32·2	122	43·9	166
A	90	—	—	8·35	34·6	24·7	103	34·2	142
CH_4	90	—	—	9·99	45·1	—	—	31·3	140
C_6H_6	323	—	—	3·74	38·0	13·0	143	~27	~180 †

* v_m is in c.c. and A in sq.m. on that weight of clay equivalent to 1 g. of Na^+-clay, complete exchange being assumed.

† Since the intercalated benzene molecules have a different orientation with respect to the sheet from those sorbed externally, a different molecular area was used.[3]

there could be intercalation only between some widely separated sheets. In the major part of the clay the interlamellar separation is, from the *X*-ray study, obviously too low. If additional expansion did occur this would, in accordance with our previous experience,[2,3] be expected to result in irreversibility of the isotherms persisting to low pressures. However, hysteresis at low pressure was not observed with methane, and was noted only to a very slight extent with oxygen, in NH_4^+-montmorillonite (Fig. 2). The slopes of the isotherms above v_m further support the view that there is little intercalation of these gases (Section 3).

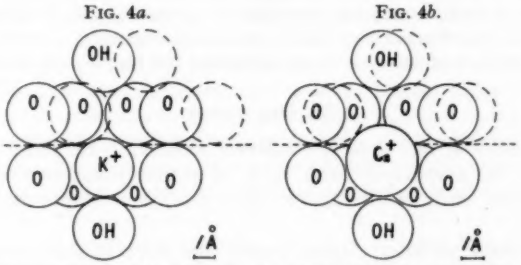

FIG. 4. *Simplified representation of the freedom of superposition of adjacent sheets in* K^+- *and* Cs^+-*montmorillonites without separation of the sheets. This will affect the proportion of expanded clay in each form.*

In the sorption of benzene at 323° K irreversibility was observed persisting to low pressures (Figs. 2 and 3), and therefore some additional lattice expansion is thought to occur. Nevertheless, the *X*-ray diffraction patterns for these clays show no substantial shift of the diffuse first-order line in the presence of benzene vapour at relative pressures ranging from 0·06 to ~1. This indicates that expansion can still involve only a small portion of the clay, presumably that already having a large sheet separation in the outgassed state. That penetration is not complete is also supported by the amounts of benzene sorbed by these clays, as compared with sorption by the alkylammonium forms.[2,3]

Sorption of water on the NH_4^+-clay gives an interesting isotherm (Fig. 2). Adsorption solely upon external surfaces is followed by a small stepwise rise, recalling the intercalation of the first layer in the Na^+-clay,[1] but at a higher relative pressure. No second layer is observed. The *X*-ray diffraction photograph shows lattice expansion but the lines remain diffuse indicating still that only part of the clay has expanded. The hysteresis loop is of the form previously found where lattice expansion occurs.[1-3]

(2) *External Surface Area and Particle Size of the* Cs^+*-Clay.*—Even allowing for a small amount of interlamellar sorption of oxygen, nitrogen, and argon on the Cs^+-clay, the isotherms indicate that the external surface of the Cs^+-form is several times that of the natural form and therefore that particle size must have decreased. A similarly high surface area for Cs^+-montmorillonite was found by Mooney, Kennan, and Wood.[7] The clay derivatives formed here were not ground, and so rupture of the particles normal to the sheets is unlikely to have occurred. Therefore any increase in external surface area on exchange from Na^+ to Cs^+ must be an increase in *sheet* and not *edge* area. Since the total external sheet and edge area of the Na^+-clay is ~20 m.²/g. and that of the corresponding amount of Cs^+-clay is ~90 m.²/g., more than 70 m.²/g. of this Cs^+-clay area must be external *sheet* area compared with less than 20 m²/g. on the Na^+-clay. This represents a marked decrease in average particle thickness. All particles being assumed to be of uniform thickness in each case, the decrease in thickness would be from $\geqslant$32 sheets for the Na^+-clay to $<$8 sheets for the Cs^+-form. It is not thought that there is a general decrease in particle thickness to ~8 sheets, but rather that some single sheets partly or wholly peel off. Thus if a 30-sheet thick particle exfoliates 4 single sheets, the exposed sheet area is increased fivefold while the average particle thickness is reduced to 6 sheets.

Since individual sheets may be widely separated when in aqueous suspension during ion-exchange,[8] the change in particle thickness may be due to differences in the tendency of the

[7] Mooney, Keenan, and Wood, *J. Amer. Chem. Soc.*, 1952, **74**, 1367.
[8] Norrish, *Discuss. Faraday Soc.*, 1954, **18**, 120.

sheets to coalesce as the gel dries after exchange. This will depend on several factors: (1) charge density of the sheets, which will be approximately constant macroscopically for the sample used throughout this research: (2) the charge on the exchange-ion, again constant in the present experiments; (3) ion size; (4) the liquid from which the gel is dried, *e.g.*, water, methanol, or acetone. Factors (3) and (4) are inter-related. In drying from water the cationic radii are those of the hydrated ions. Thus the screening of charge is greater for the hydrated Na^+ ion than for the Cs^+ ion. One might therefore expect that, if there is complete dispersion of the clay in the ion-exchanging solution, larger crystallites would form from the Cs^+-montmorillonite suspension with consequent decrease in external surface. However, most of the ion-exchanged derivatives formed were dried finally from alcohol, acetone, or ether, and this might cause the formation of small Cs^+-clay aggregates but larger ones of organic forms.

(3) Discussion

(a) *The Significance of the Slope of Isotherms above* v_m.—In many sorption isotherms the portion above the monolayer value v_m is of almost constant slope. In a series of fairly similar sorbents, such as the clays studied here, these slopes may be related to the process of sorption.

On a sorbent where no intercalation occurs, the slope of the isotherm above the v_m value indicates the formation of multilayers and should in some measure be proportional to v_m. This is a simplified picture in which such features as the condensation of sorbates in inter-particle crevices are ignored. Where intercalation does occur and is complete at or near the v_m value (as derived from the B.E.T. equation [9]) the slope of the isotherm will still be proportional to the *external* area of the sorbent. The existence of medium-sized capillaries in which limited multilayer sorption could occur would complicate this situation but will be ignored. If, on the other hand, the calculated v_m is lower than the true monolayer value and intercalation occurs above v_m, then the slope of the isotherm in this region will be greater than that for multilayer formation on the external surface alone.

The series of sorbents studied have external surfaces which are quite similar in character and on which the tendencies to form multilayers of argon or oxygen will be similar. Therefore, in those systems where intercalation is complete at v_m, it should be possible to calculate the external areas, the slope on the Na^+-form where sorption occurs only upon external surfaces being known. It has been suggested, however, that in the sorption of most molecules in the alkylammonium clays intercalation is not complete at the calculated v_m and therefore calculation of external area has not been possible by this means.[3] Nonetheless by applying these criteria it is still possible to differentiate between cases of purely external sorption and partly internal, partly external sorption.

If we express sorption in the region above v_m by the empirical expression $v - v_m = kAp$, where A is the surface sorbing above v_m, then $\delta v/\delta p = kA$. Then for sorption which is solely external $\delta v/\delta p \ll v_m$. This will not hold where intercalation occurs. Table 2

Table 2.

Clay derivative	Sorption of O_2 at 90° K			Sorption of A at 90° K		
	$\frac{\delta v}{\delta p}$	v_m	$v_m/(\delta v/\delta p)$	$\frac{\delta v}{\delta p}$	v_m	$v_m/(\delta v/\delta p)$
Na^+	0·5	0·58	1·16	—	—	—
NH_4^+ *	1·0	1·0	1·0	1·0	1·0	1·0
Cs^+	4·1	3·3	0·8	3·4	3·0	0·89
$MeNH_3^+$	2·0	4·5	2·25	1·8	4·1	2·3
$Me_2NH_2^+$	0·8	3·8	4·75	1·0	4·2	4·2
Me_3NH^+	1·0	3·7	3·7	1·0	4·2	4·2
Me_4N^+	1·6	4·3	2·7	1·9	4·4	2·3

* v_m and $\delta v/\delta p$ have been taken arbitrarily as 1·0 for the NH_4^+-clay.

summarises relevant data and suggests that the conditions of sorption do not differ markedly on the Na^+-, NH_4^+-, and Cs^+-clays. Since it was earlier established that there

is no intercalation of oxygen or argon in the Na^+-clay, this appears to be largely true for the NH_4^+- and Cs^+-forms. On the other hand, for the organic clays where intercalation occurs the values of $v_m/(\delta v/\delta p)$ are all substantially greater than unity.

(b) *Ion Fixation.*—We have given as one reason for the diffuse d_{001} lines obtained in the *X*-ray diffraction photos of NH_3^+- and Cs^+-montmorillonites the sinking of these ions into the hexagonal holes in the sheet surfaces with the varying degrees of lattice shrinkage which this permits in a structure of randomly superposed sheets. While benzene is intercalated by both clays (Section 1, c) the quantity sorbed is only a fraction of that which is sorbed when the interlamellar area is freely available for sorption.[2,3] This is supported by the *X*-ray diffraction photographs of the benzene–clay systems which do not differ appreciably from those of the outgassed clays. Again, in the sorption of water on NH_4^+-montmorillonites, although there is a shift of the d_{001} line in the *X*-ray pattern the line remains diffuse and the interlamellar spacing lower than expected if general swelling occurred. Finally, no change in the *X*-ray pattern occurs when we attempt to re-exchange to the Na^+-form a sample of Cs^+-montmorillonite which has been outgassed.

These observations may indicate "fixation" of NH_4^+ and Cs^+ ions in montmorillonite after outgassing even at room temperature. Fixation of these ions has been noted elsewhere.[5,10,11] However, when the published investigations of fixation of the alkali and

TABLE 3.

Cation	r(Å) [17]	Estimates of fixation * 1	2	3	4	5	6
Li^+	0·60	<20% Fixation	N.f.	F.	—	F.	F.
Mg^{++}	0·65	30%	,,	,,	—	,,	—
Na^+	0·95	20%	,,	N.f.	N.f.	—	—
Ca^{++}	0·99	<20%	,,	,,	F.	—	—
Sr^{++}	1·13	28%	,,	,,	—	N.f.	—
K^+	1·33	55%	F.	,,	—	—	—
Ba^{++}	1·35	45%	N.f.	,,	—	N.f.	—
NH_4^+	1·48	50%	,,	—	—	—	—
Rb^+	1·48	50%	F.	,,	—	—	—
Cs^+	1·69	42%	N.f.	,,	—	—	—

* F. = fixation; N.f. = no fixation.

Conditions of fixation.

1. Miami loam (essentially montmorillonite) dried at 100°, rehydrated for 24 hr., then exchanged with HCl: results not absolute.[10]
2. Montmorillonite dried at 105° then exchanged with NH_4OAc; alternatively dried and swelling with glycerol measured, in which case only K^+ appeared to be fixed.[12]
3. Montmorillonite heated to 100°, 200°, 330°, 430°, 540°, and 640°, then soaked in glycerol and *X*-rayed. Li^+ and Mg^{++} fixed after heating to 330°. The other ions were not fixed after heating to 430°.[13]
4. Change in hydration of Ca^{++} clay after heating to 350°.[14]
5. Samples heated to 100°, 200°, 300°, etc., then rehydrated, and the dehydration–temperature curve determined gravimetrically.[15]
6. Li^+-montmorillonite air-dried at 125° no longer swells in water.[16]

alkaline-earth cations in montmorillonite and related minerals are compared with the theories put forward to explain them, there appears to be little agreement. Table 3 summarises some of this work. The main reasons for this disagreement must be that

[9] Brunauer, Emmett, and Teller, *J. Amer. Chem. Soc.*, 1938, **60**, 309.
[10] Page and Baver, *Proc. Amer. Soil Sci. Soc.*, 1940, **4**, 150.
[11] van der Marel, *Soil Sci.*, 1954, **78**, 163.
[12] Wear and White, *ibid.*, 1951, **71**, 1.
[13] Greene-Kelly, *Clay Minerals Bull.*, 1952, **1**, 221; 1953, **2**, 52.
[14] Mering, *Trans. Faraday Soc.*, 1946, **42**, *B*, 205.
[15] Garcia, *Anales real. Soc. espan. Fis. Quim.*, 1949, **45**, *B*, 1183; 1951, **47**, *B*, 357.
[16] Hofmann and Klemen, *Z. anorg. Chem.*, 1950, **262**, 95.
[17] Pauling, "The Nature of the Chemical Bond," Cornell, 1940.

different clay samples have been used and that differing conditions of ion fixation and several methods of measuring fixation have been employed.

Differences in ion fixation appear to depend upon factors which come under two general headings.

(i) Properties of the clay mineral affecting all the cationic forms. These include the charge density of the clay sheets, its distribution between octahedral and tetrahedral layers, and the size of the platelets. The exact nature of these effects is uncertain. The interaction of the penetrating sorbate with the aluminosilicate sheets will also be important.

(ii) Factors differing in the various cationic forms: (*a*) Effective cation radius; this will depend upon the conditions of drying the clay, *e.g.*, low-temperature drying may account for those cases where Li^+ and Mg^{++} have been found not to be fixed. The radius of the cation will control its ability to sink into the haxagonal holes in the sheet surface (Fig. 1). This is turn gives rise to differences in the balance between other factors. (*b*) The electrostatic bonding of the ion with the sheets. (*c*) The energy of interaction of the cation with the penetrating sorbate. (*d*) The intersheet spacing of the dehydrated clay which affects the amount of lattice expansion required for penetration.

As the radius of the ion increases it will sink less deeply into the holes in the sheet surface and thus come less close to the main seat of negative charge in the octahedral layer so that there is a decrease in the electrostatic bonding of the ion to the sheet. Up to Sr^{++}, with ions sunk in only one sheet, it will be possible for the clay to collapse completely to give the minimum d_{001} spacing no matter how the sheets are oriented laterally. Above this radius a proportion of the clay will have a d_{001} spacing greater than the minimum. If we assume a constant degree of randomness of lateral orientation of the sheets in the various cationic forms then incompleteness of lattice collapse will increase with increasing ion diameter above 2·4 Å, the depth of the holes (Fig. 4). This in turn affects the amount of additional lattice expansion required for penetration by the sorbate. Then the energy of interaction of ion with sorbate will fall from Li^+ to Cs^+ as radius increases and will also vary with cation charge. The balance of this energy term with those associated with the factors mentioned previously will vary from one sorbate to another. Thus an ion might be fixed with respect to glycerol but not to water. These seem to be some of the most important factors involved. Others, such as the steric suitability of certain cations for co-ordination with the oxygen atoms of the clay sheets, have been dealt with elsewhere.[12] It can be concluded that complete understanding of cation fixation requires more extensive experimental work than has yet been carried out.

One of us (J. S. S. R.) wishes to acknowledge the award of a Scientific Research Fellowship during the period in which this work was carried out.

Imperial College of Science, London, S.W.7. [*Received, May 8th,* 1958.]

780. *A Revision of the Structural Assignments for the Geometrical Isomers of 3-Methyl-5-phenylpentadienoic Acid.*

By Richard H. Wiley.

Re-investigation of the geometrical isomers of 3-methyl-5-phenylpentadienoic acid has shown that the compound, m. p. 125°, formerly assigned the *cis*-2 : *trans*-4-structure is a molecular complex of the isomers of m. p.s 158° and 160°. On the basis of their physical properties and their infrared and ultraviolet absorption characteristics these two isomers are now assigned the *cis*-2 : *trans*-4- (II) and the *trans*-2 : *trans*-4-structure (I) respectively. This reassignment makes possible a new interpretation of the steric course of the Reformatsky reaction and of the mechanism of the decarboxylation by which the isomers are prepared as well as the clarification of several inconsistencies and apparent abnormalities previously noted.

The assignment of *cis-trans*-structures to the known isomers of 3-methyl-5-phenylpentadienoic acid has recently been re-examined [1] in detail and used [2] as a basis, with some qualifications and reservations, for assigning structures to intermediates in the synthesis of vitamin A. The *trans*-2 : *trans*-4-structure has been assigned to the isomer of m. p. 160° on the basis that it is the most stable product and is obtained by iodine-catalysed isomerisations of the other two forms. The isomer, m. p. 125°, has been assigned the *cis*-2 : *trans*-4-structure because it is obtained in a Reformatsky reaction with benzylideneacetone and ethyl bromoacetate under conditions which with other carbonyl compounds give lower-melting acids isomerisable to, and often accompanied by, their higher melting forms. The isomer, m. p. 158°, being isomerisable to the 160° form, was assumed to be of necessity a *cis*-form also and has, therefore, been assigned the *trans*-2 : *cis*-4 structure even though the ultraviolet absorption data require an improbable coplanar hindered *cis*-structure. It is also necessary to postulate a rather improbable formation of this hindered *trans*-2 : *cis*-4-structure by opening of the lactone ring in 5 : 6-dihydro-4-methyl-6-phenyl-2-pyrone (III) which has been reported [3,4] as a product of the Reformatsky reaction between benzaldehyde and ethyl γ-bromosenecioate.

In addition to these considerations which cast some doubt on the reliability of the assignments, problems have also been encountered in assigning probable structures to the apparent isomers obtained with cinnamylidene analogues [5] of the phenyl structures and with the isoprenoid structure, β-methyl-γ-*iso*pentylideneglutaconic acid [6] and in explaining the course of the decarboxylation of γ-arylidene-β-methylglutaconic acids.[7] To explain the stereochemical course of the decarboxylation it has been necessary to postulate that with the arylidene derivatives no inversion takes place while with the ionylidene, and presumably other alkylidene types, inversion occurs at both of the double bonds. Inversion at the double bond from which the carboxyl is removed can be explained but there appears to be no precedent for the accompanying inversion at the adjacent centre of unsaturation.

It has now been observed that the " isomer," m. p. 125°, is actually a molecular complex of the 158° and 160° isomers. In these studies the 160° isomer has been obtained as previously described [1] by the iodine-catalysed isomerisation of the 158° isomer and from the mixture of products obtained from the Reformatsky reaction of ethyl bromoacetate with benzylideneacetone. The 158° isomer has been obtained from the Reformatsky reaction

[1] Cawley and Nelan, *J. Amer. Chem. Soc.*, 1955, **77**, 4130.
[2] Robeson, Cawley, Weisler, Stern, Eddinger, and Chechak, *ibid.*, p. 4111.
[3] Fuson and Southwick, *ibid.*, 1944, **66**, 679.
[4] Harper and Oughton, *Chem. and Ind.*, 1950, 574.
[5] Petrow and Stephenson, *J.*, 1950, 1310.
[6] Wiley and Ellert, *J. Amer. Chem. Soc.*, 1957, **79**, 2266.
[7] Cawley, *ibid.*, 1955, **77**, 4125.

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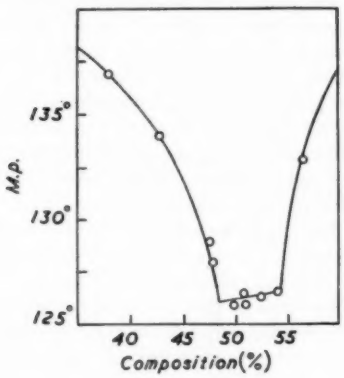
of ethyl γ-bromosenecioate with benzaldehyde and by decarboxylation of γ-benzylidene-β-methylglutaconic acid. The 125° complex has been obtained from the mixture obtained from the benzylideneacetone Reformatsky reaction and, now for the first time, by recrystallisation of a mixture of equal amounts of the 158° and 160° isomers. The 125° complex has also been obtained from the mother-liquors as the more soluble product of the iodine-catalysed isomerisation of the 158° isomer to the 160° isomer. The 125° sample prepared from the two isomers shows no depression of melting point on admixture with a sample isolated from the Reformatsky reaction and gives an infrared spectrum identical with that of the Reformatsky product. Esterification of the 125° isomer with diazomethane gives a mixture of dimethyl esters, liquid at room temperature as is also the mixture of the dimethyl esters, m. p.s 42° and 37°, obtained by esterification of the 158° and 160° isomers.

Further evidence for the existence of a molecular complex, m. p. 125—126°, is available from the melting point–composition diagram (see Figure) for mixtures of the isomers, which shows that the 50% composition is not a simple, single eutectic point. The



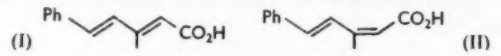
Phase diagram for (*left*) cis-2 : trans-4- *and* (*right*) trans-2-trans-4-*forms of* 3-*methyl*-5-*phenylpentadienoic acid.*

existence of a maximum in the curve is not clearly shown by the available data. It appears that the depression in melting point produced by either of the isomers on the complex is too slight to be detected by the usual melting-point measurements. This is consistent with the fact that no previous report of a depression in melting point for the complex on admixture with either isomer has been recorded.

With the information that the "isomer," m. p. 125°, is a molecular complex, it is now possible to assign structures to the two isomers which eliminate most, if not all, of the above-mentioned difficulties as well as certain other apparent contradictions in the literature describing the preparations of these compounds. The complex, m. p. 125°, has been described as the initial product obtained from the Reformatsky reaction of ethyl bromoacetate with benzylideneacetone. Three laboratories [1,8,9] have reported that this reaction gives the 125° complex: three others [10,11,12] that it gives the 160° isomer. The 160° isomer has also been prepared by the iodine-catalysed isomerisation of either the 125° or the 158° isomer. This indicates an isomerisation under conditions used by those who failed to obtain the 125° isomer caused either by the use of excess of hot mineral acid, as has been previously suggested,[1] or by the iodine added to initiate the Reformatsky reaction. However, the benzylideneacetone is certainly in the *trans*-configuration [13] and the

[8] Kuhn and Hoffer, *Ber.*, 1932, **65**, 651.
[9] Heilbron, Jones, Julia, and Weedon, *J.*, 1949, 1823.
[10] Shchukina and Rubstov, *Zhur. obshchei Khim.*, 1948, **18**, 1645.
[11] Kohler and Heritage, *Amer. Chem. J.*, 1910, **43**, 475.
[12] von Auwers and Heyna, *J. prakt. Chem.*, 1923, **105**, 361.
[13] Lutz and Jordan, *J. Amer. Chem. Soc.*, 1950, **72**, 4090.

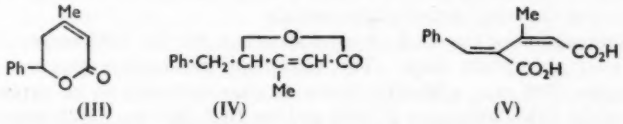
Reformatsky reaction may be assumed to give a mixture of the *cis*-2- and *trans*-2-isomers. It has been recorded [8] that this type of Reformatsky reaction does in fact give mixtures of isomers. In this event the normal product of this reaction is a mixture of the *trans*-2 : *trans*-4- (I) and the *cis*-2 : *trans*-4-isomer (II) which is isolated as the 125° molecular



(I) (II)

complex. If, however, conditions are such that the *cis*-2 : *trans*-4-isomer is isomerised to an appreciable extent the only product which can be isolated pure will be the more insoluble *trans*-2 : *trans*-4-isomer.

This explanation requires that the 158° isomer has the *cis*-2 : *trans*-4 configuration (II). This is not inconsistent with the available information about its formation as the product of the benzaldehyde–γ-bromosenecioate Reformatsky reaction.[3,4,14] This gives a mixture of unsaturated esters which has been separated into two fractions before saponification to the acids. The lower-boiling ester has been reported [3,4] to give the 160° isomer: it seems likely that it consists of one or both of the *cis*-4-isomers which are readily isomerised to the *trans-trans*-form during isolation. The higher-boiling ester is reported [3] to give the 158° isomer and this is apparently correct but only partly so as it has now been observed that it is possible to obtain impure samples of the 125° complex from the mother-liquors. The δ-lactone (III) that has previously been obtained [3,4] as a by-product of this Reformatsky reaction can now be viewed as undergoing ring opening to the *cis*-2 : *trans*-4-structure which is more readily understandable than it was on the previous structural assignment which required a rather improbable ring opening to the hindered *trans*-2 : *cis*-4-structure. Unsaturated lactones are known to open with double-bond inversion at the αβ-position to give the *trans*-2 unsaturated acid but the *cis*-orientation is retained under favourable conditions.[15] The γδ-double bond would be expected to be formed in the *trans*-configuration by analogy with the base-catalysed β-elimination of a β-acetoxy-group which forms the *trans*-product.[16] It appears that the most probable product of such a ring opening would be the *cis*-2 : *trans*-4-structure in keeping with the present revised structure of the product. Although this lactone has not been isolated in the present studies of this reaction, there does occur in all of the ester fractions a carbonyl band at 1764 cm.$^{-1}$ indicative of an



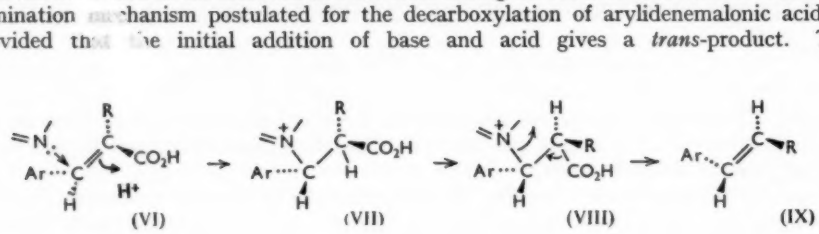
(III) (IV) (V)

unsaturated γ-lactone-carbonyl group. This, coupled with the failure to achieve δ-lactonisation of the dicarboxylic acid, under conditions which readily give δ-lactonisation in the alkylidene series, indicates that the structure of this lactone is that of the γ-lactone (IV). There is no clear-cut evidence of terminal methylene groupings in the infrared spectra for the products of this reaction. This confirms the previous report [4] that no α-alkylation occurs with the senecioate reaction although it does [17] with the analogous γ-bromocrotonate.

The 158° isomer has also previously been obtained [1] by decarboxylation of γ-benzylidene-β-methylglutaconic acid (V) catalysed by lutidine–copper acetate. This has also been confirmed. If the *cis*-2 : *trans*-4-structure is correct for the decarboxylated product, the glutaconic acid is most likely to be either *cis*-2 : *trans*-4- or *cis*-2 : *cis*-4-compound (V) and in the latter case undergoes inversion on decarboxylation. The *trans*-4-structure for the glutaconic acid can be eliminated with some assurance as the ultraviolet

[14] Ziegler, Schumann, and Winkelmann, *Annalen*, 1942, **551**, 120.
[15] Eisner, Elvidge, and Linstead, *J.*, 1953, 1372.
[16] Linstead, Owen, and Webb, *J.*, 1953, 1211.
[17] Jones, O'Sullivan, and Whiting, *J.*, 1949, 1415.

absorption (...3; ε 17,600) is typical of a *trans*-cinnamic acid structure which is present in ... *trans*-4-acid (V). The inversion of the *cis*-4- to the *trans*-4-form is consistent with the fo...tion of the more stable *trans*-form during the reaction and with the addition-elimination mechanism postulated for the decarboxylation of arylidenemalonic acids [18] provided th... initial addition of base and acid gives a *trans*-product. The



mechanism is shown in (VI—IX). This involves *trans*-addition of the base and acid (VI to VII); rotation to bring the carboxyl *trans* to the lutidine before elimination (VIII); and *trans*-elimination to (IX) in which the phenyl group is *trans* to the residual carbon chain.

The assignment of the *cis*-2-structure to the benzylideneglutaconic acid is consistent with the known ease [6] with which alkylideneglutaconic acids are converted into δ-lactones and with their conversion into anhydrides. The failure of the cinnamylidene analogue to form an anhydride, previously taken [7] as indicating a *trans*-2-structure is apparently not determining. Models show that lactonisation and anhydride formation are equally favoured structurally. The phenyl analogue fails to lactonise with acetic acid under conditions successfully used with the alkylidene analogues. It is decarboxylated to *trans*-3-methyl-1-phenylbutadiene rather than to the lactone when the potassium salt of the dicarboxylic acid is heated with acetic acid. On this basis the β-methyl-γ-*iso*-pentylideneglutaconic acid isomers previously described [6] are probably the *cis*-2 : *cis*-4-isomer and the *trans*-2 : *cis*-4-isomer formed with excess of alkali. It is known that alkali converts *cis*- into *trans*-β-methylglutaconic acid.[19] Also it is not unusual that the *cis*-2-form which, by analogy with β-methylglutaconic acid itself, would be the higher-melting, more insoluble form is the form isolated from the condensation starting with either the *cis*- or *trans*-form of dimethyl β-methylglutaconate.

Further confirmation of the *cis*-2 : *trans*-4-structure for the 158° isomer is to be found in the ultraviolet absorption data. The ultraviolet absorption maxima for the 125° molecular complex (306 mμ; ε 30,400) shows its characteristics to be approximately the mean of those of the 158° (308 mμ; ε 27,700) and the 160° (307 mμ; ε 33,800) isomer. The non-existence of a third isomer with identical absorption characteristics removes the necessity of postulating that one of these is a 4-*cis*-structure which, because it absorbs at the same wavelength as the 4-*trans*-forms, must be coplanar. Models indicate that such a coplanar form for the 4-*cis*-structure is so highly hindered as to be quite improbable. The ultraviolet absorption data for the methyl esters prepared from the acids with diazomethane are consistent with those for the acids. The ester from the 125° complex is a liquid with $\lambda_{max.}$ 310 mμ (ε 32,000), intermediate in intensity and wavelength maximum between the ester, m. p. 36°, from the 160° isomer ($\lambda_{max.}$ 308; ε 37,600) and the ester, m. p. 42°, from the 158° isomer ($\lambda_{max.}$ 312; ε 28,300). There are isosbestic points at 242 and 332 mμ, again evidence that the 125° product is a complex of the other two. One and possibly two isosbestic points at 245 and 328 mμ are to be seen in the ultraviolet absorption data for the acids.[1] The ultraviolet absorption data for the methyl hexa-2 : 4-dienoates also show [20] an isosbestic point in the curves for the *cis*-2 : *trans*-4-, the *cis*-*cis*-, and the

[18] Corey and Fraenkel, *J. Amer. Chem. Soc.*, 1953, **75**, 1168.
[19] Feist, *Annalen*, 1906, **345**, 79.
[20] Allan, Jones, and Whiting, *J.*, 1955, 1862.

trans-trans-acids which indicates that the supposed *cis*-2 : *trans*-4-acid of m. p. 31—34° is a complex of the *cis-cis*-, m. p. 82°, and the *trans-trans*-acid, m. p. 134°.

It is to be noted that the principal absorption maximum for the *cis*-2 : *trans*-4-ester occurs at significantly longer wavelengths than that for the *trans-trans*-ester. This is the third such sorbic acid type in which such effects have been observed. Methyl *cis*-2 : *cis*-4-sorbate [20] and the *cis*-2 : *trans*-4-dienoate [21] both absorb at longer wavelengths than do their respective *trans-trans*-isomers. *cis*-Crotonic acid also absorbs at a longer wavelength than does the *trans*-isomer. This is true even though the length of the chromophore in the *cis-trans*-isomer (5·45 Å) is less than that of the *trans-trans*-isomer (6·0 Å). These observations indicate that such shifts are not exclusively associated with terminal *cis-trans*-isomers as has been suggested [22] to account for a similar shift in the position of the maximum for terminal *cis*-, as compared with all-*trans*-, vitamin A which does not occur in the related aldehydes in which the *cis*-bond is not the terminal bond of the chromophore.

The infrared absorption spectra for the three substances show few differences and again confirm the existence of a complex. The 125° complex shows absorption maxima at 1490, 976, 933, and 885 cm.$^{-1}$ which are present in the spectrum of the 158° isomer but are not present in that of the 160° isomer, and maxima at 1353 and 916 cm.$^{-1}$ which are present in the spectrum of the 160° isomer but not in that of the 158° isomer. With the exception of the 956 cm.$^{-1}$ maximum in the 160° isomer, there is no significant maximum in the spectra for the 158° and 160° isomers which is not present in the spectrum of the 125° complex and *vice versa*. Some of the principal bands are appreciably shifted. The statement that [1] the 158° isomer shows no absorption in the 962 cm.$^{-1}$ region is perhaps misleading since it shows a very pronounced maximum at 966 cm.$^{-1}$ with a weaker maximum at 976 cm.$^{-1}$. The 160° isomer shows maxima at 963 and 956 cm.$^{-1}$, as previously noted, indicating the presence of a *trans*-ethylenic bond. Finally, the spectra of the 125° complex as isolated and as prepared by recrystallisation of a mixture of its components are identical over the entire range. Minute traces of the component isomers present as impurities in the 125° complex are readily detected by the appearance of a maximum at 1613 cm.$^{-1}$ charac teristic of the 160° isomer and an increase in the intensity of the 885 cm.$^{-1}$ band characteristic of the 158° isomer.

This reassignment of the configurations substantiates the suggested re-interpretation [23] of the data for the product obtained from *cis*- and *trans*-β-ionylideneacetaldehyde.[1,2] The product from the *trans*-aldehyde and β-methylgutaconate has, by analogy, the *cis*-2 : *cis*-4 : *trans*-6-structure; that from the *cis*-aldehyde, the *cis*-2 : *cis*-4 : *cis*-6-structure. Decarboxylation with inversion will give the *cis*-2 : *trans*-4 : *trans*-6- and the *cis*-2 : *trans*-4 : *cis*-6-structure respectively. Iodine-isomerisations of these give the previously identified all-*trans*- and *trans*-2 : *trans*-4 : *cis*-6-vitamin A acids. This structural assignment avoids postulating that the decarboxylation of the ionylidene derivatives takes place with simultaneous inversion of the configuration at both 2- and 4-double bonds and that the decarboxylation of other alkylidene and arylidene types takes place without inversion at either double bond. It is true that slightly different reaction conditions are required for the decarboxylation of the arylidene and alkylidene types but no fundamental difference of mechanism is indicated. The inversion is further confirmed by evidence now presented that complete decarboxylation of the dicarboxylic acid gives 3-methyl-1-phenylbutadiene, m. p. 33—35°, which shows a principal ultraviolet maxima at 282 mμ (ε 41,800) corresponding to that at 280 mμ (ε 28,300) for *trans*-1-phenylbutadiene [24] and is probably, therefore, *trans*. The structures previously assigned [2] to *neo*vitamin A as the *cis*-2-isomer and the *cis*-2 : *cis*-6-vitamin A are not changed by this reconsideration of the intermediates from which they have been prepared. The basis for the assignment is, however, clarified.

[21] Crombie, *J.*, 1955, 1007.
[22] Hubbard, *J. Amer. Chem. Soc.*, 1956, **78**, 4666.
[23] Heilbron and Weedon, *Bull. Soc. chim. France*, 1958, 83.
[24] Braude, Jones, and Stern, *J.*, 1947, 1087.

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Experimental

M. p.s were taken in capillary tubes cleaned with chromic–sulphuric acid, washed with distilled water and with acetone, and dried in an oven. They were observed with a calibrated thermometer partially immersed in a stirred oil-bath and may be considered to be corrected. Precision in the reproducibility of the m. p.s of the acids is difficult to obtain since rate of heating is significant particularly with the substituted glutaconic acid which is decarboxylated at its m. p. Mixed m. p.s were run simultaneously with determinations on the separate components.

Reformatsky Reaction of Benzylideneacetone with Ethyl Bromoacetate.—This reaction was repeated by following the detailed directions given previously [1] on a 0·05-molal basis, to give as a first fraction [precipitated from boiling ligroin (b. p. 40—60°)–benzene] 1·4 g. of crystals, m. p. 124—152°, and 2·6 g. of m. p. 124—126°. Recrystallisation of the former from benzene or, preferably, ethanol gave the *trans-trans*-acid, m. p. 159—160°, mixed m. p. 127—135° with a sample of the *cis*-2 : *trans*-4 acid, m. p. 157—158°, obtained by decarboxylation. The molecular complex, purified by recrystallisation from ligroin, or ligroin with 5% of added benzene, had m. p. 125—126°. The relative amounts of the two products vary unpredictably.

Reformatsky Reaction of Benzaldehyde with Ethyl γ-Bromosenecioate.—This reaction was repeated on a 0·14-molal basis by the procedure given previously.[3] The γ-bromosenecioate, n_D^{24} 1·4995, was prepared from ethyl senecioate [25] and *N*-bromosuccinimide. No iodine was added to initiate the reaction. The distilled unsaturated ester (15·14 g.) was separated into eight fractions, b. p. 115°/3 mm. to 166°/1·5 mm. The seventh fraction, b. p. 160—166°/1·5 mm. (2 g.), was treated with saturated alcoholic potassium hydroxide (20 ml.). Acidification of the ether-extracted, diluted reaction mixture precipitated a solid which recrystallised from ethanol at room temperature to give 0·8 g. of product, m. p. 158—158·5°, which gave no depression in m. p. on mixture with a sample of the *cis*-2 : *trans*-4-acid, m. p. 157—158°, obtained by decarboxylation, and melted at 125—145° when mixed with the *trans-trans*-acid, m. p. 156—158°, obtained by the iodine-catalysed rearrangement. Further cooling of the mother-liquors gave second and third fractions of crystals. Recrystallisation of the second fraction (0·1 g.) from benzene–ligroin (b. p. 40—60°) gave crystals, m. p. 124—125°. On admixture with a sample of the molecular complex, m. p. 126—127°, obtained from the Reformatsky reaction with benzylideneacetone, a m. p. of 126—127° was observed.

The infrared absorption spectra for four of the ester fractions showed a pronounced band at 1764 cm.$^{-1}$ indicative of a γ-lactone. The band was most prominent in the seventh fraction used for the hydrolysis and least prominent in the third fraction (2·64 g.), b. p. 148—154°/2 mm. Attempts to isolate a γ-lactone by more careful fractionation were unsuccessful.

Decarboxylation of γ-Benzylidene-β-methylglutaconic Acid.—The *cis*-2 : *trans*-4-acid, m. p. 157—158°, was obtained by following the procedure given previously.[1] The lutidine solution was not evaporated before being poured into dilute aqueous acid to precipitate the crude product. 7·0 g. of γ-benzylidene-β-methylglutaconic acid gave 3·55 g. of the product, m. p. 157—158°, as the first fraction of crystals from ethanol. Recrystallisation from nitromethane gave long needles, m. p. 158—158·5°, mixed m. p. 125—135° with the *trans-trans*-acid, m. p. 156—158°, obtained by the iodine-catalysed isomerisation.

Dipotassium γ-benzylidene-β-methylglutaconate was warmed with glacial acetic acid according to the procedure given previously [6] for the conversion of γ-alkylidene-β-methylglutaconic acids into their δ-lactones. Evaporation of the ether solution of the neutral fraction deposited crystals. Fractionation gave a fraction, b. p. 76—81°/3—5 mm., m. p. 33—35°. The m. p. previously recorded [11] for 3-methyl-1-phenylbutadiene is 37° (Found: C, 90·9; H, 8·5%; *M*, 138·8. Calc. for $C_{11}H_{12}$: C, 91·6; H, 8·4%; *M*, 144·8). The ultraviolet spectrum shows maxima at 218 (ε 17,850), 225 (ε 17,400), 232 (ε 11,300), and 282 mμ (ε 41,800). 1-Phenylbutadiene [24] shows maxima at 223 (ε 12,000), 233 (ε 8500), 271 (ε 28,000), 280 (ε 28,300), 290 (ε 27,000), 305 (ε 6000). The infrared absorption spectrum shows, as the most prominent band, a maximum at 962 cm.$^{-1}$ characteristic of the *trans*-disubstituted ethylenes.

Iodine-catalysed Isomerisations of the cis-2 : trans-4- *and the Molecular Complex to the* trans-2 : trans-4-*Acid.*—Either the *cis*-2 : *trans*-4-acid, m. p. 156—158°, obtained by decarboxylation, or the molecular complex, m. p. 125—126°, when treated with iodine according to the procedure

[25] The author is indebted to Mr. P. Veeravagu for preparing this compound.

given previously [1] gives as the fraction insoluble in boiling ligroin (b. p. 40—60°) the *trans-trans*-acid, m. p. 156—157°. The mother-liquors from the isomerisation of the *cis*-2 : *trans*-4-acid gave crystals of the molecular complex, m. p. 125—126°.

Phase Diagram.—The data for the phase diagram (Figure) were obtained by the usual procedure.[26] Samples of the *trans-trans*-acid obtained from the iodine-catalysed isomerisation and the *cis-trans*-acid obtained by decarboxylation were used.

Preparation of the Molecular Complex from the Component Acids.—A mixture of equal amounts (0·6005 g.) of the *trans-trans* obtained from the Reformatsky reaction and the *cis*-2 : *trans*-4-acid obtained by decarboxylation were fused together and recrystallised from benzene to give the molecular complex, m. p. 125—126°. The infrared absorption spectrum for this sample of the complex is identical with, and superimposable on, that of the complex, m. p. 125—126°, obtained from the Reformatsky reaction with benzylideneacetone. The complex can also be obtained by recrystallisation, without previous fusion, of equal amounts of these two acids. It is necessary, however, to recrystallise the mixture with care in order to avoid contamination with traces of the components which are readily detected by the appearance of a band at 1613 cm.$^{-1}$ not present in the spectrum of the complex but characteristic of the *trans-trans*-isomer, and by an increase in intensity of the 885 cm.$^{-1}$ band which is more intense in the spectrum for the *cis*-2 : *trans*-4-isomer than it is in that of the complex. With such care the spectra are identical; otherwise they are superimposable over the entire range with the two exceptions stated. By far the most convenient procedure for obtaining crystals of the molecular complex free from excess of either component is to evaporate a benzene solution of a mixture of the components on a watch-glass. The crystals which separate at the periphery of the evaporating solution remain moist with the solution and grow as the evaporation proceeds. The liquid is replenished with additional solution or solvent to keep the growing crystals moist.

Methyl 3-*Methyl*-5-*phenyl*-cis-2 : trans-4-*pentadienoate.*—An ether solution of 3-methyl-5-phenyl-*cis*-2 : *trans*-4-pentadienoic acid (0·93 g.), m. p. 158°, prepared by the decarboxylation of γ-benzylidene-β-methylglutaconic acid, was treated with a slight excess of diazomethane in ether. The ether solution was washed with dilute aqueous alkali, dried, and evaporated. The residue crystallised on cooling. Trituration twice with cold ligroin (b. p. 40—60°) gave a residue (0·67 g.) of white crystals, m. p. 41·5—42·5°. The m. p. was not raised by recrystallisation from ligroin (Found: C, 77·0, 77·4; H, 7·0, 7·2. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%). $\lambda_{max.}$ were 232 (ε 14,350), 238 (ε 11,500) and 312 mμ (ε 28,300).

Methyl 3-*Methyl*-5-*phenyl*-trans-2 : trans-4-*pentadienoate.*—This was prepared from the *trans-trans*-acid, m. p. 160°, isolated from the mixture of products obtained in the Reformatsky reaction of benzylideneacetone with ethyl bromoacetate. A solution of the acid (0·45 g.) in ether (15 ml.) treated with ethereal diazomethane gave, after isolation as described for the *cis-trans*-ester, white crystals (0·41 g.), m. p. 35—36°. The m. p. was not raised by recrystallisation from ligroin (Found: C, 77·25, 77·43; H, 7·12, 6·90. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%). $\lambda_{max.}$ were at 308 (ε 37,600), 238 (ε 9900), and 232 mμ (ε 11,900). A mixture of this *ester* with the *cis-trans*-ester liquefied at room temperature.

Mixture of Methyl 3-*Methyl*-4-*phenyl*-trans-2 : trans-4- *and* cis-2 : trans-4-*pentadienoate.*—This was prepared from the molecular complex, m. p. 125°, isolated from the mixture of products obtained in the Reformatsky reaction of benylideneacetone with ethyl bromoacetate. Prepared and isolated as described for the component ester, a liquid product was obtained. A solution of this in ligroin (b. p. 40—60°), cooled at −78°, precipitated crystals which were separated by decantation. The liquid residue after thorough evacuation was analysed (Found: C, 77·27; H, 7·1. Calc. for $C_{13}H_{14}O_2$: C, 77·2; H, 7·0%) and had $\lambda_{max.}$ 310 (ε 32,000), 238 (ε 10,600), and 232 mμ (ε 13,800).

The infrared absorption spectra of the acids were determined as Nujol mulls, and those of the esters as liquid films, on a Grubb-Parsons DB1 double-beam recording infrared spectrometer with a type S4 monochromator and sodium chloride optics. The author is indebted to Mr. R. L. Erskine for assistance with these observations.

The ultraviolet absorption spectra were determined for ethanol solution in 1 cm. silica cells in a Perkin-Elmer recording ultraviolet spectrometer. The author is indebted to Mrs. A. I. Boston for assistance with these measurements. The carbon and hydrogen determinations were done by the micro-analytical laboratory at the Imperial College.

[26] Vogel, "A Text-book of Practical Organic Chemistry," Longmans, Green and Co., London, 2nd edn., 1951, p. 28.

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781. *Cyclic Diarsines. Part V.* Diphenyl Derivatives containing Seven-, Eight-, Nine-, and Ten-membered Diarsine Ring Systems.*

By Harry Heaney, Denys M. Heinekey, Frederick G. Mann, and Ian T. Millar.

An improved synthesis of 2 : 2′-diphenylylenebisdimethylarsine (I) is described. The diarsine reacts with methyl bromide to form mono- and di-quaternary salts under appropriate conditions. With methylene, ethylene, trimethylene, and *o*-xylylene dibromide the diarsine forms cyclic diquaternary dibromides. These salts decompose on being heated: those derived from methylene and *o*-xylylene dibromide give the expected products having respectively seven- and ten-membered di(tertiary arsine) ring systems; in contrast, the salts derived from ethylene and trimethylene dibromide decompose with contraction of the heterocyclic rings to give 9-methyl-9-arsafluorene.

The quaternising and chelating properties of the above diarsines, and the stereochemistry of the compounds so formed, are discussed.

2 : 2′-Diphenylylenebisdimethylarsine (I) was originally isolated by Heaney, Mann, and Millar [1] from the products of the action of iododimethylarsine on a complex mixture of Grignard reagents, produced by the interaction of *o*-bromoiodobenzene and excess of magnesium at 0°. However, this reaction yields six other arsines and diarsines in addition to the diarsine (I), which moreover was isolated in the lowest yield (*ca.* 1·6%) of all these products. For the further investigation of this diarsine a more convenient method of preparation was therefore sought.

We now find that 2 : 2′-dilithiodiphenyl, conveniently prepared from ethereal 2 : 2′-diiododiphenyl and metallic lithium, reacts smoothly with iododimethylarsine to give the diarsine (I) in 63% yield.

We find that 2 : 2′-diphenylylenebisdimethylarsine (I) when dissolved in an excess of cold methyl bromide readily forms a monomethobromide, but when this solution contains a trace of methanol the dimethobromide is ultimately formed. The presence of methanol is known powerfully to promote quaternisation.[2,3] The dimethobromide is also formed, in the absence of methanol, by heating a solution of the diarsine (I) in methyl bromide at 80°. A solution of the diarsine (I) in methyl iodide readily forms a dimethiodide at room temperature.

This behaviour recalls that of *o*-phenylenebisdimethylarsine, $C_6H_4(AsMe_2)_2$, and

* Part IV, Jones and Mann, *J.*, 1955, 411.

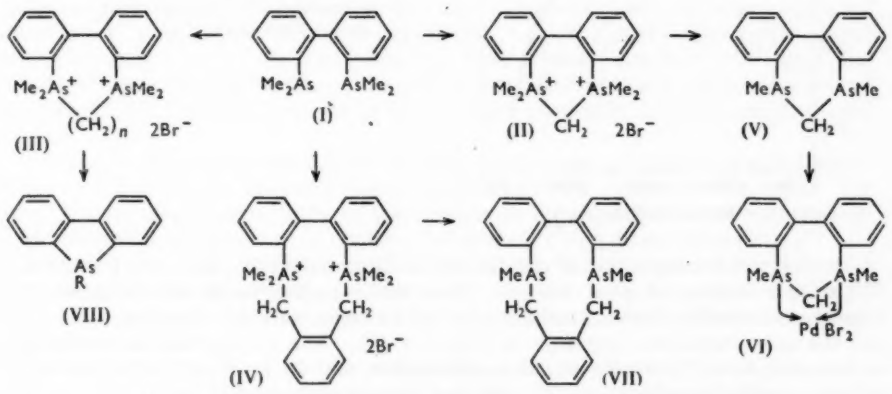
[1] Heaney, Mann, and Millar, *J.*, 1957, 3930.
[2] Menschutkin, *Z. phys. Chem.*, 1890, **6**, 41.
[3] Mann and Watson, *J. Org. Chem.*, 1948, **13**, 509.

certain related diarsines. Mann and Baker [4] have shown that this diarsine in cold methyl bromide readily forms a monomethobromide, but with methyl bromide at 100° gives a dimethobromide. Similarly a solution of this diarsine in an excess of boiling methyl iodide forms only a monomethiodide, but when heated at 100° gives the dimethiodide. In each case the quaternisation of the second tertiary arsine group requires much more vigorous conditions than those required for the first group; moreover, the melting points of the resulting salts indicate that the diquaternary compounds readily lose methyl halide when heated, to give the more stable monoquaternary salts.

It is clear, therefore, that in the monoquaternary salts of 2 : 2′-diphenylylenebisdimethylarsine (I) the deactivation of the remaining tertiary arsine group by the positive charge on the quaternary group is much less than that in corresponding salts of *o*-phenylenebisdimethylarsine, and it may be ascribed to a similar inductive effect transmitted in the diarsine (I) by a longer path.

It is of interest that 2 : 2′-diphenylylenebisdimethylamine, the nitrogen analogue of the diarsine (I), forms only a monomethiodide when heated with methyl iodide in a sealed tube at 100°.[5]

It has been shown that *o*-phenylenebisdimethylarsine undergoes ready diquaternisation with alkylene dibromides yielding cyclic diarsonium dibromides; the reaction is not limited to the formation of six-membered rings.[4,6] This reaction is clearly promoted by



the fact that the tertiary arsine groups in this diarsine are rigidly held in a favourable position by the *o*-phenylene group. Similar reactions using 2 : 2′-diphenylylenebisdimethylarsine (I) have now been investigated.

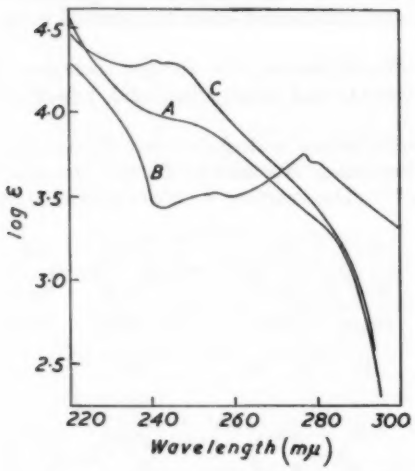
It is improbable for steric reasons that the molecule of this diarsine (I) can be coplanar: a model indicates that the angle between the planes of the benzenoid rings cannot be less than *ca.* 25°, and in conformity the ultraviolet absorption spectrum (see Figure) lacks almost entirely the characteristic diphenyl band in the 252 mμ region. Nevertheless, the rotation of the benzenoid planes beyond this angle might allow the two tertiary arsine groups to adopt suitable relative positions for diquaternisation with a range of alkylene dihalides.

Experiment has confirmed this expectation. When 2 : 2′-diphenylylenebisdimethylarsine is heated with methylene, ethylene, trimethylene, or *o*-xylylene dibromide at 100° for some hours, the corresponding tricyclic dimethobromides (II), (III; $n = 2$ or 3), and (IV), respectively, are formed in high yields. In all four cases, evidence that cyclisation

[4] Mann and Baker, *J.*, 1952, 4142.
[5] Shaw and Turner, *J.*, 1933, 135.
[6] Glauert and Mann, *J.*, 1950, 682.

had occurred and that the products were not the isomeric monoarsonium bromides was provided by the formation of the corresponding dipicrates when cold ethanolic solutions of the dibromides were treated with ethanolic sodium picrate.

The stereochemistry of cyclic diarsonium salts of the types (II), (III; $n = 2$ or 3), and (IV) is noteworthy. Construction of models of the cations indicates that the heterocyclic rings are buckled and almost strainless; and that the benzenoid rings of the diphenyl system are not coplanar, and could not become so without great distortion of normal bond angles and lengths. This lack of coplanarity, and the twisted heterocyclic rings which it entails, causes these salts to possess molecular dissymmetry, and they should therefore be resolvable into optically active forms. These resolutions are now under investigation.



Ultraviolet absorption spectra, in n-*hexane, of*:
(*A*) 2 : 2′-*diphenylylenebisdimethylarsine* (I).
(*B*) 9-*methyl*-9-*arsafluorene* (VIII; R = Me).
(*C*) 5 : 7-*dimethyl*-5 : 7-*diarsa*-1 : 2-3 : 4-*dibenzo*-cyclo*heptadiene* (V).

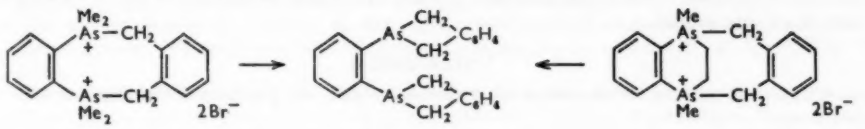
The thermal decomposition of the diarsonium dibromides (II), (III; $n = 2$ or 3), and (IV) reveals features of great interest. Thus the seven-membered ring dibromide (II) decomposes smoothly above its melting point, at 0·15 mm., with loss of methyl bromide to give the seven-membered ring ditertiary diarsine (V). This diarsine has been identified by (*a*) analysis, (*b*) molecular-weight determination, and (*c*) by its ready reaction with potassium palladobromide to give the chelated covalent compound (VI).

Thermal decomposition of the *o*-xylylene salt (IV) follows a similar course, yielding the cyclic diarsine (VII) in which the ten-membered heterocyclic ring has remained intact.

The diarsines (V) and (VII) were converted into their quaternary dimethopicrates, which were identical with those prepared directly from the parent dimethobromides (II) and (IV) respectively. This affords strong evidence that these methobromides have the structure indicated and are not in fact the " dimeric " tetra-arsonium tetrabromides.

However, thermal decomposition of the eight-membered ring dibromide (III; $n = 2$) follows a novel course; smooth decomposition at the melting point gives 9-methyl-9-arsafluorene (VIII; R = Me) in high yield, together with traces of a bromoarsine, almost certainly 9-bromo-9-arsafluorene (VIII; R = Br). The presence of a bromoarsine was shown by the intense yellow colour developed when the crude product, dissolved in acetone, was mixed with a solution of sodium iodide in the same solvent.[4] However, the small proportion of the bromoarsine present, together with the high tendency of the 9-methyl-9-arsafluorene to crystallise during distillation, rendered separation of these two compounds difficult. The crude product was therefore treated with ethereal methylmagnesium iodide, which readily gave the pure 9-methyl-9-arsafluorene (VIII; R = Me), m. p. 41—41·5°, in overall yield of 69%.

Aeschlimann, Lees, McCleland, and Nicklin [7] have prepared 9-methyl-9-arsafluorene, and give m. p. 46°; however, they were unable to obtain fully satisfactory analytical values. The identity of the arsine prepared by thermal decomposition of the dibromide (III; $n = 2$) was established as 9-methyl-9-arsafluorene by (*a*) analysis, (*b*) the formation of derivatives, in particular the quaternary methiodide and the corresponding methopicrate, and (*c*) by the similarity of the ultraviolet absorption spectrum of this arsine (Figure) with that of 9-*p*-tolyl-9-arsafluorene, recorded by Campbell and Poller.[8]



(IX) (XI) (X)

This formation of a bromo-arsine during the thermal decomposition of a heterocyclic methylarsonium bromide is not novel. The *o*-phenylene analogue of (III; $n = 2$) yields both 1 : 4-dimethyl- and 1-bromo-4-methyl-ethylene-*o*-phenylenediarsine (Mann and Baker [4]); 5 : 10-dihydro-5 : 10-dimethylarsanthren dimethobromide similarly gives 5-bromo-5 : 10-dihydro-10-methylarsanthren (Jones and Mann [9]).

The contraction of an eight-membered ring containing two quaternary arsonium groups in a 1 : 4-position on thermal decomposition, to yield a product having the arsenic atoms contained in five-membered rings, has been recorded previously by Jones and Mann,[10] who showed that the dibromides (IX) and (X) readily gave *o*-phenylenebis-(2-*iso*-arsindoline) (XI), but the formation of this product necessarily involved intermolecular reactions.

This contrasts with the ring contraction (III; $n = 2$) ⟶ (VIII) now recorded, which furthermore involves an unusually ready fission of an aryl carbon–arsenic bond. The second arsenic atom is eliminated in this transformation ultimately as trimethylarsine, which has been characterised as its dinuclear complex with palladium dibromide.

The nine-membered ring dibromide (III; $n = 3$) also decomposes with the formation of 9-methyl-9-arsafluorene in 49% yield, and contamination with a bromoarsine is barely detectable. In this decomposition the second arsenic atom is eliminated almost certainly as dimethylvinylarsine.

The structural factors in the dibromides (II), (III; $n = 2$ and 3), and (IV) which determine their type of thermal decomposition (*i.e.*, with or without ring contraction) remain uncertain. It appears significant, however, that decomposition with ring contraction occurs only in the dibromides (III; $n = 2$ or 3) which have flexible bridging groups, whereas the heterocyclic ring, which is rigid in the dibromide (II) and has very limited flexibility in the dibromide (IV), remains intact during the decomposition. Furthermore, the ethylene and the trimethylene bridge in the dibromides (III; $n = 2$ or 3) both possess a methylene group containing hydrogen atoms in the β-relation to the arsenic atoms: such hydrogen atoms may be essential if this exceptional ring-contraction involves an elimination mechanism similar in general type to that shown, for example, by several cyclic quaternary phosphonium bromides.[11] This mechanism is of course quite different from that of the normal thermal dissociation of arsonium halides containing at least one alkyl group.

It is clearly unlikely that the decomposition of the dibromide (III; $n = 2$) proceeds by

[7] Aeschlimann, Lees, McCleland, and Nicklin, *J.*, 1925, **127**, 66.
[8] Campbell and Poller, *Chem. and Ind.*, 1953, 1126; *J.*, 1956, 1195.
[9] Emrys R. H. Jones and Mann, *J.*, 1955, 411.
[10] *Idem*, *J.*, 1955, 405.
[11] Beeby and Mann, *J.*, 1951, 411; Mann and Millar, *J.*, 1951, 2205; Hart and Mann, *J.*, 1955, 4107; Mann, Millar, and Watson, *J.*, 1958, 2516.

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initial decomposition to ethylene dibromide and 2 : 2′-diphenylylenebisdimethylarsine (I) followed by loss of trimethylarsine and ring closure of the diarsine (I), since the dimethiodide of the diarsine (I) decomposes smoothly and normally at 260°/0·05 mm. to give the diarsine (I).[1] It is also noteworthy that the formation of the arsafluorene, under these relatively vigorous conditions of thermal decomposition, affords further evidence for the high stability of this ring system.

We are now investigating the formation and thermal decomposition of salts formed by the quaternisation of the cyclic diarsines (V) and (VII) with alkyl halides and with alkylene and other dibromides.

Experimental

Compounds are colourless unless otherwise described. M. p.s were determined on a Kofler hot stage.

2 : 2′-*Di-iododiphenyl.*—Diphenyleneiodonium iodide (58·5 g.), prepared as described by Lothrop [12] in 56% yield, was heated in an oil-bath at 215—220° for 30 min. The residue was extracted with ether (Soxhlet), and the extract percolated through a short column of chromatographic alumina to remove coloured impurities not readily removable by charcoal: evaporation of the solvent followed by recrystallisation from ethanol gave 2 : 2′-di-iododiphenyl, m. p. 110° (40 g., 68%).

2 : 2′-*Diphenylylenebisdimethylarsine* (I).—This preparation was performed throughout under nitrogen. A solution of 2 : 2′-di-iododiphenyl (7·84 g.) in ether (100 c.c.) was added dropwise to fine lithium foil (1 g.) covered by ether (10 c.c.) at such a rate that the mixture boiled gently, and the complete mixture was then boiled under reflux for 30 min. The resulting solution of 2 : 2′-dilithiodiphenyl was decanted from insoluble material. Iododimethylarsine (9·4 g., 2 mols.) in benzene (50 c.c.) was added dropwise during 15 min. to the cooled solution, which was then boiled under reflux for 1 hr., cooled, and hydrolysed with cold air-free water. The organic layer was separated and dried (Na_2SO_4), the solvents were evaporated, and the residue was distilled under reduced pressure in nitrogen, giving the fractions: (*a*) diphenyl, b. p. 80—85°/0·7 mm. (0·6 g., 20%), m. p. and mixed m. p. 66—67° after two recrystallisations from methanol; (*b*) 2 : 2′-diphenylylenebisdimethylarsine, b. p. 146—152°/0·7 mm. (4·4 g., 63%). The diarsine prepared in this way may be used for the preparation of quaternary salts, but gives high carbon values on analysis, owing to contamination with diphenyl. It may be purified by conversion into the dimethiodide, followed by thermal decomposition of the recrystallised salt, and then has b. p. 110°/0·05 mm., m. p. 46—46·5°.[1]

Quaternary Salts of 2 : 2′-*Diphenylylenebisdimethylarsine.*—A solution of the diarsine (I) in an excess of methyl bromide was set aside in a sealed tube at room temperature for 1 hr. with occasional shaking, crystals rapidly separating. The excess of methyl bromide was allowed to evaporate and the residue when recrystallised from ethanol–light petroleum (b. p. 80—100°) gave the *monomethobromide monohydrate*, m. p. 240—241° (decomp.) (Found: C, 42·55; H, 5·0. $C_{17}H_{23}BrAs_2,H_2O$ requires C, 42·9; H, 5·3%).

To prepare the dimethobromide, a similar solution of the diarsine (I) was heated in a sealed tube at 80° for 3 hr. Removal of the excess of methyl bromide and recrystallisation of the residue from ethanol–light petroleum (b. p. 60—80°) gave the dimethobromide dihydrate, m. p. and mixed m. p. 292—294° (decomp.) (lit.,[1] m. p. 292—294°). This salt was also prepared by confining a solution of the diarsine in an excess of methyl bromide containing a trace of methanol in a sealed tube at room temperature for 4 hr.

When a solution of the diarsine (I) in an excess of methyl iodide was set aside at room temperature, salt formation rapidly occurred. The residue, after evaporation of the excess of methyl iodide and crystallisation from methanol, gave the dimethiodide, m. p. and mixed m. p. 289—290° (decomp.) (lit.,[1] m. p. 286—288°) (Found: C, 33·2; H, 3·85. Calc. for $C_{18}H_{26}I_2As_2$: C, 33·5; H, 4·0%).

5 : 5 : 7 : 7-*Tetramethyl*-5 : 7-*diarsonia*-1 : 2-3 : 4-*dibenzo*cyclo*heptadiene Dibromide* (II).—The diarsine (I) (1 g.) was heated with methylene dibromide (0·48 g., 1 mol.) in a sealed tube at 100° for 6 hr. The product when washed with ether and recrystallised from ethanol–light petroleum (b. p. 80—100°) gave the *dibromide tetrahydrate*, m. p. 224—225° (decomp.) (Found: C, 36·9; H, 4·85. $C_{17}H_{22}Br_2As_2,4H_2O$ requires C, 36·4; H, 4·95%). The corresponding *dipicrate* was

[12] Lothrop, *J. Amer. Chem. Soc.*, 1941, **63**, 1187.

deposited when cold ethanolic solutions of the above dibromide and of sodium picrate were mixed and formed yellow crystals, m. p. 283—285°, from water or from ethanol containing a small amount of acetone (Found: C, 41·65; H, 3·05; N, 9·95. $C_{29}H_{26}O_{14}N_6As_2$ requires C, 41·9; H, 3·15; N, 10·1%).

5 : 5 : 9 : 9-*Tetramethyl*-5 : 9-*diarsonia*-1 : 2-3 : 4-*dibenzo*cyclo*nonadiene Dibromide* (III; n = 3).—The diarsine (I) (1 g.) was heated with trimethylene dibromide (0·52 g., 1 mol.) in a sealed tube at 100° for 4 hr. The crystalline product, purified as before, gave the hygroscopic *dibromide monohydrate*, m. p. 261—262° (decomp.) (Found: C, 39·2; H, 4·85. $C_{19}H_{26}Br_2As_2,H_2O$ requires C, 39·2; H, 4·85%). The corresponding *dipicrate*, prepared as above, formed yellow crystals, m. p. 201—203°, from ethanol containing a small amount of acetone (Found: C, 42·8; H, 3·8; N, 9·95. $C_{31}H_{30}O_{14}N_6As_2$ requires C, 43·3; H, 3·5; N, 9·75%).

5 : 5 : 10 : 10-*Tetramethyl*-5 : 10-*diarsonia*-1 : 2-3 : 4-7 : 8-*tribenzo*cyclo*decatriene Dibromide* (IV).—The diarsine (I) (1·04 g.) and *o*-xylylene dibromide (0·76 g., 1 mol.) in methanol (1 c.c.) were heated in a sealed tube at 100° for 4 hr. The methanol was then evaporated, and the crystalline residue washed with ether and recrystallised from ethanol, giving the *dibromide monohydrate*, m. p. 209—210° (decomp.) (1·25 g., 80%) (Found: C, 44·2; H, 4·55. $C_{24}H_{28}Br_2As_2,H_2O$ requires C, 44·7; H, 4·7%). The corresponding *dipicrate*, prepared as above, formed yellow crystals, m. p. 225—227°, from water or from ethanol containing a small amount of acetone (Found: C, 46·3; H, 3·7; N, 9·1. $C_{36}H_{32}O_{14}N_6As_2$ requires C, 46·8; H, 3·5; N, 9·1%).

Thermal Decompositions.—(A) *The dibromide* (II). The dibromide (2·5 g.) was placed in a distillation flask fitted with a capillary intake, air-condenser, and a receiver connected in turn to a trap cooled in liquid oxygen, and evacuated to 0·15 mm. whilst nitrogen was led through the capillary. Heating in an air-bath at 250° caused smooth decomposition, yielding a colourless syrupy distillate (1·26 g.) and no residue. A sample of the distillate dissolved in acetone developed no colour when mixed with a solution of sodium iodide in the same solvent. Crystallisation of the distillate from ethanol gave 5 : 7-*dimethyl*-5 : 7-*diarsa*-1 : 2-3 : 4-*dibenzo*cyclo*heptadiene* (V), m. p. 95·5—96° (Found: C, 51·9; H, 4·7%; *M*, ebullioscopic in acetone, 355. $C_{15}H_{16}As_2$ requires C, 52·05; H, 4·65%; *M*, 346). The ultraviolet absorption spectrum of this diarsine in *n*-hexane is given in the Figure.

The diarsine, when boiled with aqueous ethanolic potassium palladobromide, deposited the yellow crystalline *dibromodiarsinepalladium* (VI), m. p. 318—319° (decomp.) (Found: C, 29·8; H, 2·8. $C_{15}H_{16}Br_2As_2Pd$ requires C, 29·4; H, 2·65%). No satisfactory solvent could be found for recrystallisation.

To prove that the ring system had not undergone rearrangement during decomposition, the diarsine (V) was heated with an excess of methyl iodide at 100° for 3 hr. The crude dimethiodide was washed with ether, and its ethanolic solution treated with ethanolic sodium picrate; the dipicrate corresponding to (II) was deposited (m. p. and mixed m. p. 283—285° after recrystallisation from water).

(B) *The* 5 : 5 : 8 : 8-*tetramethyl*-5 : 8-*diarsonia*-1 : 2-3 : 4-*dibenzo*cyclo*octadiene dibromide* (III; n = 2). The powdered dibromide (7 g.), prepared as described earlier,[1] was heated in the above-mentioned apparatus at 0·1 mm. in an oil-bath at 210—215°, decomposition of the salt occurring smoothly and being complete in 45 min. The distillate (3·08 g.), at first colourless and ultimately faintly golden, showed a high tendency to crystallise and effective fractionation on redistillation proved impracticable.

Solutions of the distillate and of sodium iodide in acetone when mixed developed an intense yellow colour, indicating the presence of a bromoarsine.

The distillate, dissolved in ether, was therefore mixed with an excess of ethereal methylmagnesium iodide under nitrogen, in order to convert any bromoarsine (VIII; R = Br) into the tertiary arsine (VIII; R = Me). Hydrolysis with aqueous ammonium chloride followed by separation of the organic layer, drying (Na_2SO_4), and one distillation in nitrogen gave 9-methyl-9-arsafluorene, b. p. 125°/0·05 mm., m. p. 41—41·5° (lit.,[7] m. p. 46°) (2·97 g., 69%) (Found: C, 64·5; H, 4·9. Calc. for $C_{13}H_{11}As$: C, 64·5; H, 4·6%); $\lambda_{max.}$ (log ε) in *n*-hexane (see Figure), 255 (3·52) and 277 (ε 3·75); $\lambda_{min.}$ (log ε) 242 (3·43) and 259 mμ (ε 3·51). The maximum and minimum at the longer wavelengths probably correspond to those observed at 279 mμ (log $\varepsilon_{max.}$ 4·15) and 264 mμ ($\log_{10} \varepsilon_{min.}$ 4·06) in the spectrum of 9-*p*-tolyl-9-arsafluorene in *cyclo*hexane, determined by Campbell and Poller.[8]

XUM

A solution of 9-methyl-9-arsafluorene in an excess of methyl iodide was set aside at room temperature, salt formation rapidly occurring. The precipitate, when washed with ether and recrystallised from ethanol, gave 9 : 9-*dimethyl*-9-*arsoniafluorene iodide monohydrate*, m. p. 206—207° (decomp.) (lit.,[7] m. p. 190° for the anhydrous salt) (Found: C, 41·5; H, 3·8. $C_{14}H_{14}IAs,H_2O$ requires C, 41·8; H, 4·0%). The anhydrous *picrate* formed yellow crystals, m. p. 214·5—215·5°, on recrystallisation from ethanol containing a small amount of acetone (Found: C, 49·4; H, 3·35; N, 9·2. $C_{26}H_{16}O_7N_3As$ requires C, 49·5; H, 3·35; N, 8·7%).

A solution of 9-methyl-9-arsafluorene in ethanol, when boiled with aqueous-ethanolic potassium palladobromide, rapidly deposited yellow crystals of *dibromobis*-(9-*methyl*-9-*arsafluorene*)*palladium*, decomp. *ca.* 320° (Found: C, 41·7; H, 3·15. $C_{26}H_{22}Br_2As_2Pd$ requires C, 41·6; H, 3·0%). No satisfactory solvent could be found for recrystallisation.

The trap, which had been cooled in liquid oxygen during the thermal decomposition, was allowed to warm to room temperature. It was then warmed to 60—70° whilst a stream of nitrogen was passed through it, the effluent gas being passed by means of glass-to-glass connections through gently boiling aqueous-ethanolic potassium palladobromide, extra portions of the latter being occasionally added to ensure an excess, indicated by the deep red colour of the solution. Concentration of the solution and cooling afforded orange-red crystals which, recrystallised from ethanol, gave dibromobis(trimethylarsine)-μμ′-dibromodipalladium, m. p. and mixed m. p. 232° (Found: C, 9·6; H, 2·6. Calc. for $C_6H_{18}Br_4As_2Pd_2$: C, 9·3; H, 2·3%).

(C) *The dibromide* (III; $n = 3$). The powdered dibromide (12 g.), in the above apparatus at 0·05 mm., was heated in an air-bath, initially at 230°; decomposition occurred smoothly to give a pale yellow liquid distillate. The temperature was ultimately raised to 260°, the distillate then becoming more discoloured.

A sample of the crude distillate gave only a slight yellow colour with sodium iodide in acetone.

Fractionation of the distillate in nitrogen gave 9-methyl-9-arsafluorene (VIII; R = Me), b. p. 110°/0·2 mm. (2·5 g., 49%) which readily crystallised and when recrystallised from methanol had m. p. 42°. This compound was identified by its ultraviolet absorption spectrum, and by conversion into its methiodide which in turn afforded the yellow crystalline 9 : 9-dimethyl-9-arsoniafluorene picrate, m. p. and mixed m. p. 215°. Another sample of the arsine, boiled with aqueous ethanolic potassium palladobromide, gave the yellow crystalline dibromobis-(9-methyl-9-arsafluorene)palladium, decomp. *ca.* 320°.

The contents of the trap cooled in liquid oxygen were treated as in the previous experiment, giving red-brown crystals (from ethanol), m. p. 270°, probably solvated *dibromobis*(*dimethylvinylarsine*)-μμ′-*dibromodipalladium* (Found: C, 13·3; H, 2·45. $C_8H_{18}Br_4As_2Pd_2,0{\cdot}5C_2H_6O$ requires C, 13·2; H, 2·55%).

Dibromobis(*ethyldimethylarsine*)-μμ′-*dibromodipalladium*, which in a solvated form would give very similar analytical values, was prepared in the usual way, and formed red-brown crystals, m. p. 207° from ethanol (Found: C, 12·1; H, 3·1. $C_8H_{22}Br_4As_2Pd_2$ requires C, 12·0; H, 3·15%).

(D) *The dibromide* (IV). The powdered dibromide (1·5 g.) contained in a bulb-tube at 0·05 mm. was heated in an oil-bath at 210°; smooth decomposition gave an arsine which distilled when the temperature was raised to 235°. Crystallisation of the solidified distillate from ethanol gave 5 : 10-*dimethyl*-5 : 10-*diarsonia*-1 : 2-3 : 4-7 : 8-*tribenzo*cyclo*decatriene* (VII), m. p. 110—111° (Found: C, 60·0; H, 4·95%; *M*, cryoscopic in benzene, 402. $C_{22}H_{22}As_2$ requires C, 60·5; H, 5·05%; *M*, 436). To prove that the ring system had not undergone rearrangement during the decomposition, the diarsine (VII) was heated with an excess of methyl toluene-*p*-sulphonate under nitrogen for 8 hr. Removal of excess of the reagent with ether gave a syrup which failed to crystallise but with ethanolic sodium picrate gave the quaternary dipicrate, m. p. and mixed m. p. 225—227° (from water), analogous to (IV).

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782. *Physicochemical Studies on Starches. Part XVI.* The Molecular Weight and Apparent Molecular-weight Distribution of Rabbit-liver Glycogen.*

By W. A. J. Bryce, C. T. Greenwood, and I. G. Jones.

The effects of extraction with hot alkali and cold trichloroacetic acid on the molecular weight of rabbit-liver glycogen have been examined. Molecular weights have been obtained by both sedimentation–diffusion and light-scattering measurements. Apparent distribution curves of sedimentation coefficients for various glycogen samples have been calculated. Glycogen extracted by cold trichloroacetic acid appears to be more representative of native glycogen than that isolated by hot alkali. Difficulties in the sub-fractionation of glycogen are discussed.

Our recent physicochemical studies [1] of various glycogen samples have indicated that polydispersity † is quite common, and that good agreement between the molecular weights derived from sedimentation–diffusion and light-scattering measurements is unusual. Some of the factors involved for rabbit-liver glycogen are described here, as a preliminary to use of the results as standards for the hydrodynamic behaviour of branched glucosans. The molecular weight of this glycogen from sedimentation measurements has been reported [1,2] to be about 6×10^6, but in recent light-scattering work by Stetten, Katzen, and Stetten [3] molecular weights of $11—80 \times 10^6$ were obtained when extraction was with cold trichloroacetic acid, whilst alkaline extraction gave products of molecular weights $2—6 \times 10^6$. However, determination of the molecular weight of glycogen by only one physicochemical method is inadequate.[1] In the present work, we isolated the glycogen by different methods and investigated the products by (1) sedimentation-velocity measurements, to give an apparent molecular-weight distribution, and (2) turbidimetric measurements, to give the weight-average molecular weight ($\overline{M}_w$).

For use of glycogen as a standard for hydrodynamic behaviour, fractions with a narrow molecular-weight distribution are preferable. The sub-fractionation of glycogen has therefore also been examined.

Experimental

Isolation.—Livers from freshly killed rabbits were minced and divided into two portions. The glycogen in one portion was isolated by the classical Pflüger method of extraction with 30% sodium hydroxide solution and subsequent reprecipitation with ethanol and 80% acetic acid.[1] Glycogen isolated by this method is termed *OH*-glycogen. {Typical analytical figures were: glucose, 99% (on hydrolysis and estimation of the reducing power with alkaline potassium ferricyanide [4]); $[\alpha]_D^{16}$ +194° (*c* 0·2% in H_2O); conversion into maltose on β-amylolysis, 41%.} The other portion was extracted with trichloroacetic acid at 2° and the glycogen-product purified as described by Stetten, Katzen, and Stetten.[3] Glycogen isolated by this method is termed *TCA*-glycogen. {Typical analytical figures were: glucose, 98%; $[\alpha]_D^{16}$ +190 (*c* 0·2% in H_2O); conversion into maltose on β-amylolysis, 45%.}

Sedimentation–Diffusion and Light-scattering.—These were carried out as described in Part XII of this series,[1] the solvent for the glycogen samples being 0·1M-sodium chloride.

Diffusion. These measurements were carried out in the Antweiler microelectrophoresis and diffusion apparatus at 20°. The concentration at a point *x* in a diffusion column is a function [5]

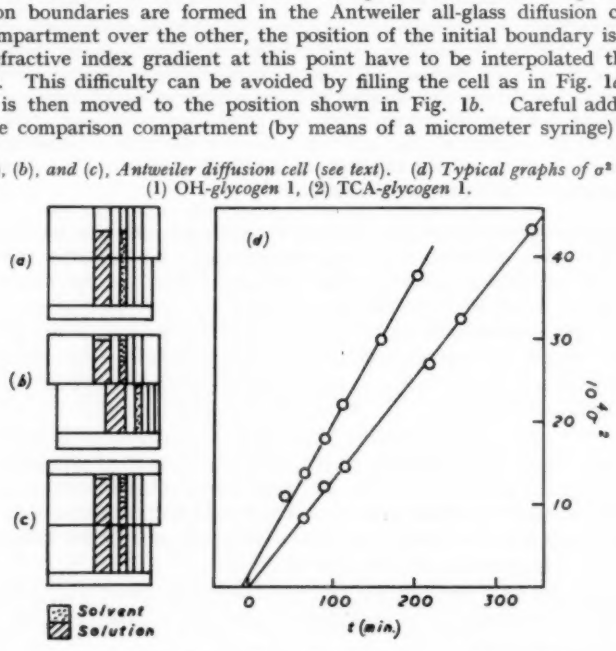
* Part XV, *J.*, 1958, 3558.

† The term "polydisperse" is used to describe a polymer system containing more than one component, whilst "polymolecular" denotes a chemically homogeneous polymer having a variation in molecular weight.

[1] Bryce, Greenwood, Jones, and Manners, *J.*, 1958, 711.
[2] Greenwood, *Adv. Carbohydrate Chem.*, 1952, **7**, 289; 1956, **11**, 335.
[3] Stetten, Katzen, and Stetten, *J. Biol. Chem.*, 1956, **222**, 587.
[4] Lampitt, Fuller, and Coton, *J. Sci. Food Agric.*, 1955, **6**, 656.
[5] Longsworth, *Ann. N.Y. Acad. Sci.*, 1945, **46**, 211.

of $x/\sqrt{t}$, and hence, if x is decreased by 10, the time required to reach a given concentration is reduced by 100. The duration of the experiment can therefore be considerably decreased if dn/dx can be measured at very small values of x. In practice, as there is usually an upper limit of dn/dx which can be measured, this can be achieved only by employing a cell with a short optical path, dn/dx for given values of x and t being then proportionately decreased. Hence, with a microcell a much shorter time is required for diffusion experiments. When solvent–solution boundaries are formed in the Antweiler all-glass diffusion cell by simply sliding one compartment over the other, the position of the initial boundary is obscured and readings of refractive index gradient at this point have to be interpolated throughout the measurements. This difficulty can be avoided by filling the cell as in Fig. 1*a*. The upper compartment is then moved to the position shown in Fig. 1*b*. Careful addition of more solution to the comparison compartment (by means of a micrometer syringe) will raise the

FIG. 1. *(a), (b), and (c), Antweiler diffusion cell (see text). (d) Typical graphs of σ^2 against t for* (1) OH-*glycogen* 1, (2) TCA-*glycogen* 1.



boundary from its interfacial position. The cell is then moved into position 1*c*, after removal of the residual solvent and its replacement by solution. In this manner, extremely sharp boundaries were formed. The refractive index gradient (dn/dx) in the liquid column was obtained either by arithmetical differentiation of the results from manually scanning the column with the Jamin interferometer, or by photography of the gradient obtained directly by the Schlieren optical-system attachment. For high concentrations of glycogen, the boundaries were too sharp to be measured satisfactorily by the interference method; in other respects the results from both methods of observation were the same.

Diffusion coefficients were evaluated by either the area–maximum ordinate method (D_a) or the second-moment method (D_m), where [6]

$$D_a = \left[\int_{-\infty}^{+\infty} y \,.\, dx\right]^2 \Big/ 4\pi t(y_{max.})^2 = A^2/4\pi t(y_{max.})^2$$

and

$$D_m = \left(\int_{-\infty}^{+\infty} x^2 y \,.\, dx\right) \Big/ \left(2t\int_{-\infty}^{+\infty} y \,.\, dx\right) = \sigma^2/2t$$

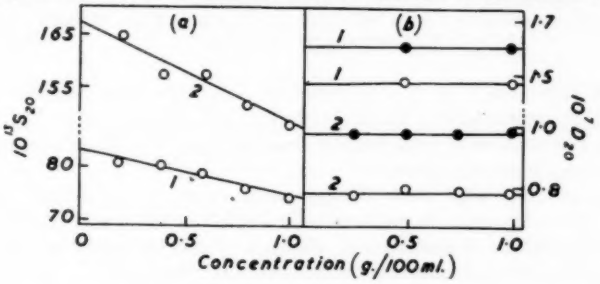
Here, x = the distance perpendicular to the boundary; $y = dn/dx$, the gradient of the refractive index; t = the time in seconds; σ^2 = the second moment of the curve; and A = the area. In all cases, the graph of σ^2 against t was linear and intercepted the t-axis at, or close (at a negative value) to, the origin (see Fig. 1). The time values used in calculations of diffusion coefficient were corrected for any apparent displacement of the zero time. Values are thought to be accurate to $\pm 3\%$ at any given concentration.

[6] Neurath, *Chem. Rev.*, 1942, **30**, 357.

Ultracentrifugation. These measurements were made with a Spinco ultracentrifuge. Runs were usually carried out at 20,000 r.p.m. and at concentrations of 2·5—8·0 g./l. A speed of 8000 r.p.m. was necessary in studying the apparent molecular-weight distribution of *TCA*-glycogen. Sedimentation coefficients (S_{20}) were evaluated from measurements of the movement of the mode of the sedimentation diagram [*i.e.*, $(dn/dx)_{max.}$] in the usual manner. S_{20} values therefore represent the sedimentation coefficient of the molecular species apparently present in the largest amount.

Light-scattering. High-speed centrifugation could not be used to clarify the solutions before turbidity measurements, as rapid sedimentation of very large particles occurred (see below). Clarification was again achieved by filtration of concentrated solution through sintered glass (G4) under gravity. (Millipore filters and G5 filters were not satisfactory and tended to remove polysaccharide from solution.) For each sample, measurements were made at 4 or 5 concentrations in the range 1—10 × 10^{-5} g./ml. obtained by successive addition of the concentrated filtered solution to optically clear solvent. (The concentration of the original filtered solution was obtained by hydrolysis and estimation of the liberated glucose with

FIG. 2. (*a*) *Plot of* S_{20} *against* c *for* (1) OH-*glycogen* 1 *and* (2) TCA-*glycogen* 1.
(*b*) *Plot of* D_{20} *against* c *for* (1) OH-*glycogen* 1 *and* (2) TCA-*glycogen* 1; ● D_m *values*; ○ D_a *values*.



alkaline ferricyanide.[4]) This procedure gave reproducible turbidities and dissymmetries. Molecular weights were calculated from the equation: $Hc/\tau = 1/M(P_{90°}) + 2Bc/\boldsymbol{RT}$, where $H = 32\pi^3n^2(dn/dc)^2/3\lambda^4\boldsymbol{N}$; $(P_{90°})$ = a particle scattering factor, which was calculated on the assumption that the molecules were spherical; [1] B = the solute–solvent interaction parameter; dn/dc = the refractive index increment, which was taken [1] as 0·146 (c in g./ml.) for glycogen in 0·1M-sodium chloride at 546 mμ. Within experimental error, Hc/τ and I_{45}/I_{135} were found to be independent of c for the range of concentrations examined. The term $2B(P_{90°})c/\boldsymbol{RT}$ was therefore negligible.

The partial specific volume ($\bar{V}$) of glycogen was taken [1] as 0·62.

Subfractionation.—This was attempted by cooling a 0·1% solution in 15% (v/v) aqueous ethanol, and by differential centrifugation as described by Stetten, Katzen, and Stetten.[3] Stepwise addition of ethanol to aqueous solutions at room temperature was also tried.

Results and Discussion

Concentration Dependence of S_{20} *and* D_{20}.—Sedimentation coefficients for rabbit-liver glycogen have been determined previously, but early investigations [7,8] were limited to only one concentration, Bridgman [7] stating that the concentration-dependence of S_{20} was less than the experimental error. However, recently we have confirmed Larner, Ray, and Crandall's results [9] that the concentration-dependence is real.[1] For the range of concentrations studied, $S_{20} = (S_{20})_0(1 - k_sc)$. Representative data are shown in Fig. 2*a*. By the method of least squares, values of k_s of 0·12 and 0·11 for *OH*- and *TCA*-glycogen respectively were obtained.

[7] Bridgman, *J. Amer. Chem. Soc.*, 1942, **64**, 2349.
[8] Bell, Gutfreund, Cecil, and Ogston, *Biochem. J.*, 1948, **42**, 405.
[9] Larner, Ray, and Crandall, *J. Amer. Chem. Soc.*, 1956, **78**, 5890.

For diffusion coefficients also, early data [7,8] were restricted to one concentration. Bridgman's values [7] of $D_m = 1{\cdot}1 \times 10^{-7}$ for the majority of his samples were limiting values for time-dependent measurements. Ogston and his co-workers [8] gave values of $1{\cdot}27$—$1{\cdot}21 \times 10^{-7}$, whilst Larner and his co-workers' results [9] for samples of comparable

TABLE 1. *Molecular-weight data for* OH- *and* TCA-*glycogen.*

Method	Sedimentation–diffusion		Light-scattering			
Sample	$10^{13}(S_{20})_0$	$10^{-6}\,\overline{M}_{SD}$ [a]	$10^{-6}(\tau/Hc)$ [b]	I_{45}/I_{135} [b]	$10^{-6}\,\overline{M}_\tau$	$\overline{M}_\tau/\overline{M}_{SD}$
OH-Glycogen 1	84	3·1	13·6	1·70	19·0	6·1
			4·0 [c]	1·18 [c]	4·5 [c]	1·5
,, 2	86	3·3	—	—	—	—
,, 3 ‡	94	3·9	6·9	1·20	7·8	2·0
,, 4	95	3·9	7·1	1·20	8·0	2·1
TCA-Glycogen 1	168	9·4	38·5	2·00	62 †	6·6
			40·5	1·94	63 †	
,, 2	173	9·8	90	2·40	160 †	16·0
			91	2·40	162 †	
,, 3	163	9·1	—	—	—	—

[a] Calc. from data in Fig. 4. [b] Values at infinite dilution; I_{45}/I_{135} = dissymmetry ratio.
[c] Values after centrifugation at 20,000 r.p.m. for 15 min. (Spinco ultracentrifuge. Preparative rotor A.) † Independent determinations. ‡ Values from ref. 1.

S_{20} were larger ($1{\cdot}3$—$1{\cdot}5 \times 10^{-7}$) and possessed a definite, but variable, concentration-dependence. Our experimental results (see Fig. 2*b*) suggest that the dependence is negligible. In all instances, symmetrical diffusion curves were obtained, again indicating negligible concentration-dependence.[6,10]

Comparison of OH- *and* TCA-*Glycogen with regard to Molecular Weight and its Distribution.*—The sedimentation coefficients in Table 1 indicate a large difference between *OH*- and *TCA*-glycogen. A quantitative estimate of this difference can be obtained only from the distribution of sedimentation coefficients $g(S)$, where: [7,11]

$$g(S) = (\mathrm{d}c/\mathrm{d}x)\omega^2 t x^3/c_0 x_0^2$$

where ω = angular velocity (radians/sec.), t = time (sec.) from the start of the sedimentation, x = distance (cm.) of a point in the boundary from the axis of rotation, x_0 = distance (cm.) of the meniscus from the axis of rotation, and c_0 = total concentration of the solution. An absolute distribution results only if diffusion is negligible and S is independent of c. Corrections for these effects can be made.[11,12] Here, Baldwin's method [11] has been employed to correct for diffusion and obtain apparent distributions $g'(S)$ (the calculations necessary for this distribution are detailed in Part XV). If $g'(S)$ is obtained at identical concentrations and the sedimentation behaviour of the samples is the same, the resultant curves should be comparable, although corrections for the Johnston–Ogston effect [11,13] and the concentration dependence [11] of S should ideally be applied. The $g'(S)$ curves shown in Fig. 3 emphasise the radical difference between *OH*- and *TCA*-glycogen (*e.g.*, only 8% of *OH*-glycogen 4 has $S > 150$, whilst *TCA*-glycogen 1 has 61% and *TCA*-glycogen 2 has 72%). Table 2 shows calculated values of the standard deviation, mean (or weight-average) sedimentation coefficient, and skewness. The standard deviation for *OH*-glycogen 4 calculated from Baldwin's most recent work,[14] taking into

[10] Jullander, *Arkiv Kemi Min. Geol.*, 1945, *A*, **21**, 1; Beckmann and Rosenberg, *Ann. N.Y. Acad. Sci.*, 1946, **46**, 229; Bevilacqua, Bevilacqua, Blender, and Williams, *ibid.*, p. 309.
[11] Baldwin, *J. Amer. Chem. Soc.*, 1954, **76**, 402.
[12] See, *e.g.*, refs. in article by Kinell and Rånby in "Advances in Colloid Science," Vol. III, Interscience Publ. Inc., New York, 1950; Baldwin and Williams, *J. Amer. Chem. Soc.*, 1950, **72**, 4325; Gosting, *ibid.*, 1952, **74**, 1548; Williams, Baldwin, Saunders, and Squire, *ibid.*, p. 1542; Baldwin, *J. Phys. Chem.*, 1954, **58**, 811; Williams and Saunders, *ibid.*, p. 854; Williams, Saunders, and Cicirelli, *ibid.*, p. 774; Eriksson, *Acta Chem. Scand.*, 1956, **10**, 378.
[13] Johnston and Ogston, *Trans. Faraday Soc.*, 1946, **42**, 789.
[14] Baldwin, *Biochem. J.*, 1957, **65**, 490.

account the concentration dependence of S, is the same (*i.e.*, 36S) as that calculated from the $g'(S)$ curve at 8·0 g./l. Both *TCA*-glycogens have a large positive skew; that for *OH*-glycogen is relatively small. The ratio[15] D_m/D_a (Table 2) from diffusion measurements indicated the increased polymolecularity of *TCA*-glycogen.

FIG. 3. *Plot of $g'(S)$ against S for* (1) OH-*glycogen* 4, (2) TCA-*glycogen* 1, (3) TCA-*glycogen* 2[$g'(S) = 0$ *at* $S = 1400$; *the amount of this sample with* S *between* 600 *and* 1400 *is about* 25%].

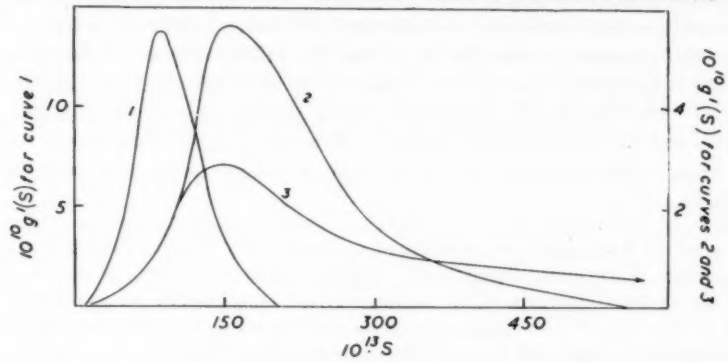
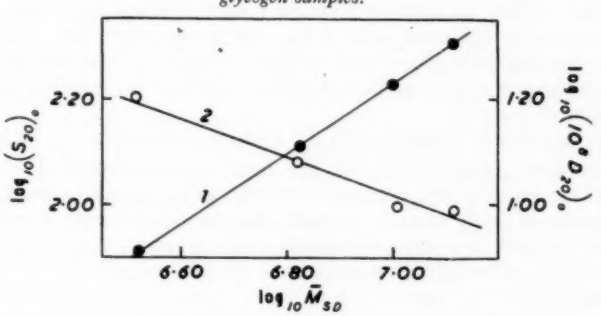


FIG. 4. *Plots of* (1) $\log_{10}(S_{20})_0$ *against* $\log_{10}\overline{M}_{SD}$, *and* (2) $\log_{10}(D)_{20})_0$ *against* $\log_{10}\overline{M}_{SD}$ *for glycogen samples.*



When molecular weights were calculated from S_{20} and D_m (to give $\overline{M}_{SD}$) for four samples, then $S_{20} \approx \overline{M}_{SD}^{0.63}$ (see Fig. 4). From Kuhn and Kuhn's results,[16] (1) $S \approx M^{\frac{1}{2}}$ for a matted coil, and (2) $S \approx M^{\frac{2}{3}}$ for a sphere, and hence glycogen may behave as essentially

TABLE 2. *Sedimentation coefficients and derived quantities from $g'(S)$ curves.*

Sample	$10^{13}S_{20}$ [a]	$10^{13}S_m$ [b]	σ [c]	Sk [d]	D_m/D_a	$10^{-4}\overline{M}_{SD}$ [e]	$10^{-4}M$ [f]
OH-Glycogen 4	87	95	34	+0·23	1·08	3·9	5·0
TCA-Glycogen 1 ...	150	220	99	+0·70	1·27	9·4	18
,, 2 ...	150	417	310	+0·87	—	9·8	45

[a] Sedimentation coefficient as measured from the mode. [b] Calc. mean sedimentation coefficient [c] Standard deviation. [d] Skewness = (mean − mode)/σ (see, *e.g.*, Yule and Kendall, "Introduction to the Theory of Statistics," Griffin, London, 1950. [e] Values from Table 1. [f] Molecular weight calc. from S_m by assuming $k_s = 0{\cdot}12$ and data in Fig. 4.

spherical particles. Similar conclusions can be drawn from the fact that $D_{20} \approx \overline{M}_{SD}^{0.37}$ (see Fig. 4), an exponent of 0·33 being expected for a sphere. It is realised these relations

[15] Gralén, Inaugural Diss., Uppsala, 1944.
[16] Kuhn and Kuhn, *Helv. Chim. Acta*, 1943, **26**, 1394.

are, at best, only approximate, as fractionated samples should have been used: this was not possible (see below). {The compact nature of the particles is confirmed by viscosity measurements. $[\eta]$ was 6·2 for *OH*-glycogen 1 and 7·1 for *TCA*-glycogen 1. (Units of concentration = g./ml.; solvent = 0·1M-sodium chloride; temperature = 22·5°.)}

Molecular weights from sedimentation–diffusion measurements on extremely polymolecular polymers are not simple averages, but depend [17] on the shape of the molecule and the methods of evaluating S and D, and hence no direct correlation is to be expected with the results of light-scattering measurements ($\overline{M}_\tau$ values) shown in Table 1.

$\overline{M}_\tau$ for *OH*-glycogen is much less than that for *TCA*-glycogen. Differences between $\overline{M}_\tau$ for *TCA*-glycogens 1 and 2 are explained by the differences in skewness of the $g'(S)$ curves. The ratio $\overline{M}_\tau/\overline{M}_{SD}$ appears to give a qualitative measure of skewness of the distribution and values are given in Table 1. Molecular weights calculated by using mean sedimentation coefficients from the $g'(S)$ curve are more comparable with $\overline{M}_\tau$ values (see Table 2).

Stability of TCA-*Glycogen.*—The effect of various reagents on the sedimentation behaviour of *TCA*-glycogen was examined to investigate whether physical aggregation was occurring. Ultrasonic experiments (which will be described in detail elsewhere) showed that under conditions which rapidly degrade amylopectin no appreciable change occurred in either S_{20} or the appearance of the leading edge of the sedimenting boundary. *TCA*-Glycogen also appeared to be stable to dilute acid and alkali at room temperature. After 72 hr., 0·5% solutions in 0·2M-potassium hydroxide and -acetic acid had the same S_{20} value as a control solution in 0·2M-sodium chloride, and there was no apparent change in the leading edge. When an aqueous solution (under air) was heated on a boiling-water bath, S_{20} was virtually the same after 1 hr. (158S ⟶ 151S), and even after 4 hours' heating, there was relatively little effect (131S). Changes in the leading edge were then apparent which did not appear to be reversible. Limited degradation or disaggregation must therefore have occurred.

The above experiments suggest that *TCA*-glycogen dissolves to form an essentially molecular dispersion. Further, $\overline{M}_\tau$ for the limit dextrin produced by the action of β-amylase had decreased by 50% compared with the 45% enzymic conversion into maltose. This is in agreement with Stetten, Katzen, and Stetten's results,[3] and suggests that aggregation was limited, as it appears unlikely that the extent of any aggregation, persisting after the 41% loss of weight on β-amylolysis, would be equivalent to that before treatment with enzyme.

However, when a 0·2% solution in 30% aqueous potassium hydroxide (under air) was heated on a boiling-water bath, S_{20} decreased rapidly and then remained constant

TABLE 3. *Sub-fractionation of* TCA-*glycogen.*

Sample:	1			2			
Method:	Cooling to 0° and centrifugation			Differential centrifugation			
Yield (%)	$10^{-6}\,\overline{M}_{SD}$ *	$10^{-6}\,\overline{M}_\tau$	$\overline{M}_\tau/\overline{M}_{SD}$	Yield (%)	$10^{-6}\,\overline{M}_{SD}$ *	$10^{-6}\,\overline{M}_\tau$	$\overline{M}_\tau/\overline{M}_{SD}$
45	10·3	66	6·4	38	—	250	—
30	7·0	55	7·9	42	12·7	90	7·1
20	8·6	50	5·8	16	8·6	13·3	1·5

* Calc. from $(S_{20})_0$ value and data in Fig. 4.

(168S ⟶ 100S in ½ hr. ⟶ 83S in 1 hr. ⟶ 86S in 4 hr.). The sedimentation diagram was then indistinguishable from that of *OH*-glycogen. A similar effect was found when heating was in a nitrogen atmosphere. *TCA*-Glycogen appears to be alkali-labile, but oxidative degradation appears to be insignificant. *OH*-Glycogen must be a degradation product relatively stable to alkali.

[17] Singer, *J. Polymer Sci.*, 1946, **1**, 445.

Effect of Isolation Procedure on Molecular Weight.—We support Stetten, Katzen, and Stetten's conclusions [3] that *TCA*-glycogen is more representative of native glycogen than *OH*-glycogen. Extraction with hot 30% potassium hydroxide solution causes obvious degradation, and molecular-weight values reported previously [1,2] for glycogens isolated from tissues by this method are undoubtedly those of degraded products. Since degradation may also have occurred during the isolation of *TCA*-glycogen,[3] the extremely high weight-average molecular weight of this material suggests that " native " glycogen may well *not be amenable to study by conventional physicochemical methods* (compare, for example, ref. 18). The difficulties involved in the study of the size of " native " glycogen are obviously very great. It should be noted, however, that for bacteria [19] and yeasts [20] *TCA*-glycogens are smaller than *OH*-glycogens, probably because the acid has only limited access and only material of low molecular weight is extracted without prior alkaline cytolysis.

The polydispersity of *OH*-glycogens apparent on sedimentation measurements varied; some were monodisperse, whilst others had both a large and a small component. Any large component could be removed by centrifugation, no significant amount (<5%) of material being lost (see sample 1, Table 1), and reprecipitation often removed the smaller component. In view of results with trichloroacetic acid, we regard polydispersity in *OH*-glycogen as due to an artefact. It is of interest that Bridgman [7] found evidence of components of low molecular weight in some of his samples.

Our previous results [1] indicated that S_{20} for *OH*-glycogen was comparable with that for glycogen isolated by boiling water. In view of the degradative effect of alkali, glycogen in the tissues which is accessible to the solvent action of hot water must be comparable in size with the degraded product.[21]

Sub-fractionation of TCA-*Glycogen.*—The results of our experiments are shown in Table 3. No significant fractionation occurred with successive addition of alcohol. The methods suggested by Stetten, Katzen, and Stetten [3] gave limited sub-fractionation, but changes in $\bar{M}_w$ are due almost entirely to changes in very large material. In no instance was there any real narrowing of the apparent molecular-weight distribution as shown by the sedimentation diagrams. Sub-fractionation of *TCA*-glycogen is obviously very difficult in view of the large molecular sizes involved.

[*Added, September 8th,* 1958.—Stetten *et al.*[22] have recently reached essentially the same conclusions as ours concerning *TCA*-glycogen.]

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THE UNIVERSITY, EDINBURGH, 9. [*Received, April 16th,* 1958.]

[18] Lazarow, *Arch. Biochem. Biophys.*, 1945, **7**, 337.
[19] Holme, Laurent, and Palmstierna, *Acta Chem. Scand.*, 1957, **11**, 757.
[20] Bryce and Greenwood, unpublished experiments.
[21] Cf. Orrell and Bueding, *J. Amer. Chem. Soc.*, 1958, **80**, 3800.
[22] Stetten, Katzen, and Stetten, *J. Biol. Chem.*, 1958, **232**, 475.

783. *The Denitration of Nitroguanidines in Strong Acids. Part I. The Correlation of Rate Constants with the Acidity Function, H_0, and Activities of Solvent Entities.*

By T. G. Bonner and J. C. Lockhart.

The rates of denitration of some nitroguanidines have been measured in an extensive range of strongly acidic media, and a difference in mechanism has been detected in sulphuric acid and perchloric acid. The empirical relation between rate constant, the acidity function H_0, and the activities of solvent species previously reported [1] for the denitration of *N*-methyl-*N'*-nitroguanidine in sulphuric acid has been confirmed for several other nitroguanidines and a new interpretation of this relation put forward. The occurrence of a minimum in the extent of denitration at equilibrium confined to the range 85—88% sulphuric acid for all the nitroguanidines investigated is discussed.

Nitration of guanidine in concentrated aqueous acid solution is reversible,[2] and rates of the reverse reaction, *i.e.*, denitration, were first obtained by Simkins and Williams.[3] Reliable measurements of the denitration rate were limited by an unfavourable equilibrium position but *N*-methyl-*N'*-nitroguanidine gave [1] accurately measurable rates in the range 71—81% of sulphuric acid. These investigations established that denitration is a first-order reaction (opposed by the second-order nitration). A parallelism was found [1,3] between the rate of the nitration and the ionisation of triarylmethanols in the same range of media which established that the nitrating entity was the nitronium ion.[4] The importance of the part played by the solvent in these equilibria is shown by the occurrence of a minimum in the extent of denitration of nitroguanidine and its *N*-methyl derivative in the same medium, *viz.* 88% sulphuric acid.

Since nitroguanidine and its *N*-methyl derivative are completely converted into their conjugate acids in below 40% sulphuric acid and are quite stable at very much higher acidities, it was assumed that denitration took place only after the addition of a second proton.[1] The mechanism first suggested [2] represented the denitration as a rate-determining ejection of the nitronium ion from the doubly-charged nitroguanidine cation

$$PH^+ + H^+ \overset{\text{fast}}{\rightleftharpoons} PH_2^{++} \overset{\text{slow}}{\rightleftharpoons} GH^+ + NO_2^+$$

where P and G represent nitroguanidine and guanidine, respectively. The species PH_2^{++} can only be present in relatively minute amount but the extent of its formation is difficult to assess. It has been shown that the stronger base, guanidine, forms detectable amounts of its doubly protonated derivative only in sulphuric acid stronger than 99% [5] but urea, a base of similar strength to nitroguanidine, does appear to become doubly charged in concentrated sulphuric acid.[6] The essential point, however, is whether the reaction proceeds uniquely through this species. This can be tested over the range of media studied by means of a relation of the type

$$\log k + H_0 = \text{constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k is the rate constant for denitration and H_0 is Hammett's acidity function.[7] Since the reactant is envisaged as carrying two positive charges, the acidity function required is

[1] Hardy-Klein, *J.*, 1957, 70.
[2] (*a*) Simkins and Williams, *J.*, 1952, 3086; (*b*) Holstead, Lamberton, and Wyatt, *J.*, 1953, **3341**; (*c*) Holstead and Lamberton, *J.*, 1953, 3349.
[3] Simkins and Williams, *J.*, 1953, 1386.
[4] Westheimer and Kharasch, *J. Amer. Chem. Soc.*, 1946, **68**, 1871.
[5] Williams and Hardy, *J.*, 1953, 2560.
[6] Hammett, "Physical Organic Chemistry," McGraw Hill Book Co., New York, 1st Edn., 1940, p. 47.
[7] *Idem, ibid.*, p. 267.

H_+ rather than H_0 but in the absence of a scale of H_+ values similar to that evaluated by Hammett for H_0, the relation can be tested only with the latter. This is acceptable, since it has been recently established that H_0 and H_+ are parallel functions of medium composition over a wide range of sulphuric acid–water mixtures.[8] The test of the mechanism proposed is that the plot of log k against H_0 should be a straight line of slope −1. In fact,

TABLE 1. *Denitration in sulphuric acid–water at* 25° (initial concn. 0·01M; k in 10^3 min.$^{-1}$).

			2-Nitramino-1 : 3 : 4-triazole			2-Nitrimino-1 : 3-diaza*cyclo*hexane			*NN*-Dimethyl-*N'*-nitroguanidine		
% H_2SO_4	A	B	k	C	D	k	C	D	k	C	D
67·0	4·36	9·52	0·42	8·80	13·16	—	—	—	—	—	—
68·0	4·46	9·67	—	—	—	0·274	8·77	13·23	—	—	—
69·7	4·59	10·03	—	—	—	0·546	8·70	13·31	0·468	8·81	13·40
70·5	4·67	10·28	1·13	8·56	13·23	0·834	8·69	13·36	—	—	—
71·8	4·78	10·54	2·09	8·44	13·22	—	—	—	—	—	—
72·8	4·84	10·76	—	—	—	2·84	8·48	13·33	1·84	8·65	13·49
74·8	4·98	11·14	12·43	8·07	13·29	7·38	8·29	13·29	4·37	8·52	13·50
76·1	5·08	11·41	—	—	—	11·8	8·29	13·39	—	—	—
78·6	5·24	11·91	63·0	7·87	13·11	36·4	8·12	13·36	—	—	—
70·2	5·27	12·05	—	—	—	—	—	—	36·4	8·22	13·49
81·9	5·33	12·45	—	—	—	—	—	—	121	8·04	13·37

			4-Methyl-2-nitrimino-1 : 3-diaza*cyclo*pentane			2-Nitrimino-1 : 3-diaza*cyclo*pentane *		
% H_2SO_4	A	B	k	C	D	k	C	D
76·1	5·08	11·41	0·514	9·62	14·70	0·302	9·84	14·92
78·6	5·24	11·91	—	—	—	1·33	9·54	14·78
79·2	5·27	12·05	1·86	9·49	14·76	—	—	—
81·2	5·33	12·37	5·16	9·33	14·66	3·99	9·34	$14·7_4$
81·9	5·33	12·45	5·95	9·36	14·69	5·98	9·34	$14·6_7$
83·3	5·38	12·72	13·6	9·21	14·60	12·07	9·27	$14·6_5$
85·1	5·42	12·99	26·0	9·15	14·57	24·3	9·20	$14·6_3$
87·5	5·40	13·31	91·9	8·95	14·35	74·0	9·04	$14·4_4$
89·9	5·30	13·51	—	—	—	191·1	8·93	$14·2_3$
92·6	5·10	13·57	—	—	—	526	8·75	13·85

A = log {H_2SO_4} + log {H_2O}; B = − (H_0 − log {H_2SO_4} − log {H_2O}); C = − (log k + H_0); D = − (log k + H_0 − log {H_2SO_4} − log {H_2O}).

* Initial concn. 0·008M.

Values of log {H_2SO_4} were obtained from Abel, *J. Phys. Chem.*, 1946, **50**, 260; 1948, **52**, 908, and of log {H_2O} from Gold and Hawes, *J.*, 1951, 2102.

TABLE 2. *Denitration in aqueous perchloric acid and in sulphuric acid–acetic acid at* 25° (initial concn. 0·01M; k in 10^3 min.$^{-1}$).

Perchloric acid–water			Sulphuric acid–acetic acid	
	N-methyl-*N'*-nitroguanidine	2-nitrimino-1 : 3-diaza*cyclo*hexane		2-nitrimino-1 : 3-diaza*cyclo*hexane
% $HClO_4$	k	k	% H_2SO_4	k
59·6	0·038	0·186	52·7	0·736
63·6	—	1·67	55·8	0·894
64·6	0·316	3·46	59·1	1·50
66·4	2·02	—	64·6	2·07
67·0	—	12·7	65·5	3·78
69·0	10·2	—	71·1	10·5
72·0	63·2	—	—	—

the slopes so far reported have been considerably removed from −1, being −1·42 for nitroguanidine[3] and −1·50 for *N*-methyl-*N'*-nitroguanidine. Bimolecular reactions were considered,[1] similar to those suggested for decarbonylation of alkylbenzaldehydes in sulphuric acid,[9] but no simple bimolecular mechanism appeared to be operative. A useful

[8] Bonner and Lockhart, *J.*, 1957, 364.

[9] Schubert and Zahler, *J. Amer. Chem. Soc.*, 1954, **76**, 1; Schubert, Donohue, and Gardner, *ibid.*, p. 9; Schubert, Zahler, and Robins, *ibid.*, 1955, **77**, 2293.

empirical relation, however, was found [1] in the reasonable constancy over the range 71—82% sulphuric acid of the summation of terms in equation (2)

$$\log k + H_0 - \log \{H_2O\} - \log \{H_2SO_4\} = \text{constant} \quad . \quad . \quad . \quad (2)$$

where the quantities in braces represent activities. Considerable difficulty is apparent in the attempts to reconcile equation (2) with a simple mechanism of denitration.[10]

It appeared desirable to examine denitration of other substituted nitroguanidines with sufficient variety of structure to ensure an extension of the range of acidity over which the reaction takes place, and also to employ strongly acid media other than aqueous sulphuric acid. A few compounds (detailed in Table 1) were suitable for measurements of rate and equilibria in aqueous sulphuric acid. 2-Nitrimino-1 : 3-diaza*cyclo*hexane (II) and *N*-methyl-*N'*-nitroguanidine were studied in aqueous perchloric acid and the former in anhydrous sulphuric acid–acetic acid also (see Table 2).

Experimental

Materials.—Sulphuric acid and perchloric acid solutions were prepared by dilution of the " AnalaR " acid with distilled water and analysed as previously reported.[3a] 100% Sulphuric acid was obtained from a weak oleum by dilution to maximum freezing point with " AnalaR " sulphuric acid. Sulphuric acid–acetic acid solutions were obtained by mixing the required weights of 100% sulphuric acid and 100% acetic acid.

Nitroguanidine was obtained by nitration of guanidine in sulphuric acid.[11] Methylnitroguanidine, m. p. 160—161°, was made from nitroguanidine as described by McKay and Wright.[12] *NN'*-Dimethyl-*N''*-nitroguanidine, m. p. 171—172°, was obtained from the mother liquor of this reaction by Hardy-Klein's method.[1] *NN*-Dimethyl-*N'*-nitroguanidine, m. p. 194—195°, was made from *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine and dimethylamine.[12]

2-Nitrimino-1 : 3-diaza*cyclo*pentane, m. p. 220—221°, 4-methyl-2-nitrimino-1 : 3-diaza*cyclo*pentane, m. p. 170—171°, and 2-nitrimino-1 : 3-diaza*cyclo*hexane, m. p. 249—250°, were prepared by the method used for methylnitroguanidine.[12] 2-Nitramino-1 : 3 : 4-triazole was made by refluxing formamidonitroguanidine with sodium carbonate.[13]

All these nitroguanidines were purified by recrystallisation to constant spectrum for kinetic work. Spectral data are given in the following paper. A commercial specimen of guanidine nitrate was recrystallised from water, then six times from water containing 10% of alcohol.

Recovery of Denitration Products.—*NN*-Dimethyl-*N'*-nitroguanidine and the diaza-*cyclo*hexane and -*cyclo*pentanes were tested by Holstead and Lamberton's method to demonstrate the formation of nitric acid. The yield in all cases was within 71—73% of theory, as had been previously found for potassium nitrate and nitroguanidine. The nitration mixture from 2-nitrimino-1 : 3-diaza*cyclo*pentane was also treated to yield the guanidine as nitrate,[3b] needles, m. p. 112—113°, identified as 2-amino-1 : 3-diaza*cyclo*pentane nitrate by conversion into the carbonate and picrate.[14]

Measurement of Reaction Velocity and Equilibrium Composition.—The optical density of a sample suitably diluted with water was measured at the absorption maximum for the particular nitroguanidine.

The absorptions of guanidine,[15] alkylguanidines,[1] and 2-aminotetrahydropyrimidine [16] are known to be negligible at 2600—2900 Å. The absorption of 2-amino-1 : 3-diaza*cyclo*pentane nitrate also was found to be negligible in this region. The nitrate ion has an extinction coefficient of ε, 2 in this region and can be neglected [1] as long as denitration is less than 95% complete.

Rate constants were obtained graphically from the kinetic equation previously employed,[1] *i.e.* $kt(2a - x_e) = 2{\cdot}3x_e \log_{10}\{a(x_e - x)/[ax_e + x(a - x_e)]\}$ where a is the initial concentration of reactant, x the concentration of the denitrated reactant at time t, and x_e the concentration

[10] Hardy-Klein, *J.*, 1957, 3312.
[11] Davis, *Org. Synth.*, Coll. Vol. I, 1948, 399.
[12] McKay and Wright, *J. Amer. Chem. Soc.*, 1947, **69**, 3028.
[13] Henry, *ibid.*, 1950, **72**, 5343.
[14] Stefanye and Howard, *ibid.*, 1955, **77**, 761.
[15] " International Critical Tables," Vol. V, McGraw Hill Book Co., New York, 1929, p. 367.
[16] Hamer, Waldron, and Woodhouse, *Arch. Biochem. Biophys.*, 1953, **47**, 272.

of the latter at equilibrium. A plot of the log term against time was a straight line to about 80% of the conversion for all compounds and media studied.

Results and Discussion

The Relation between Rate Constant and Acidity Function, H_0.—The rapid increase in rate of denitration with increasing acidity [1,3] was also found for all the compounds in Table 1. Rate constants increase approximately one-hundred fold over a 10% range of acid, for both sulphuric acid and perchloric acid solutions. The influence of acidity is only slightly less marked in sulphuric acid–acetic acid. The plots of log k against H_0 for aqueous sulphuric acid [17] are shown in Fig. 1; the slopes for all the compounds lie between −1·41 and −1·49. In aqueous perchloric acid [18] the two compounds studied, 2-nitrimino-1 : 3-diaza*cyclo*hexane and *N*-methyl-*N'*-nitroguanidine, give slopes of −0·97 and −1·09,

Fig. 1. *Variation of* log k *(denitration) with* H_0.

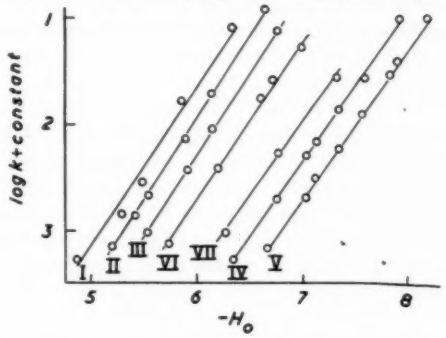
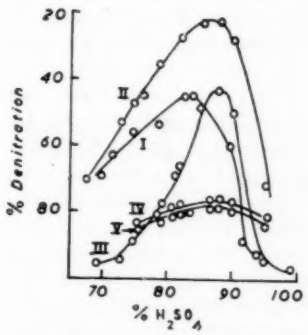


Fig. 2. % *Denitration of equilibrium.*



I, 2-Nitramino-1 : 3 : 4-triazole (−1·44); II, 2-Nitrimino-1 : 3-diaza*cyclo*hexane (−1·46); III, *NN*-Dimethyl-*N'*-nitroguanidine (−1·46); IV, 4-Methyl-2-nitrimino-1 : 3-diaza*cyclo*pentane (−1·41); V, 2-Nitrimino-1 : 3-diaza*cyclo*pentane (−1·44); VI, *N*-Methyl-*N'*-nitroguanidine (from ref. 1) (−1·49); VII, Nitroguanidine (from ref. 3) (−1·46).

Values in parentheses are of (log k)/H_0.

respectively. These results imply that denitration in perchloric acid proceeds through a diprotonated species formed in fractionally small amount [17] but that a more complex reaction occurs in sulphuric acid. Since rates in the latter are faster than required by theory, it is possible that in this medium, (*a*) catalysis occurs by some species not present in aqueous perchloric acid, or (*b*) the transition state of the reactant associates with solvent species in a manner not paralleled by the conjugate acids of the Hammett bases used to evaluate H_0.

A mechanism basically similar to that in perchloric acid cannot be excluded for sulphuric acid since previous investigators have often found justification for interpreting slopes of from −0·7 to −1·5 in terms of the simple mechanism associated with a slope of −1.[19-22] However, application of the results reported here to equation (2) showed an excellent fit in the range 67—85% sulphuric acid for all the nitroguanidines in Table 1, except 2-nitrimino-1 : 3-diaza*cyclo*pentane. With the latter the constancy is not so marked, but considerable divergence from constancy occurs only above 85% sulphuric

[17] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721.
[18] Bonner and Lockhart, *J.*, 1957, 2840.
[19] Long and McIntyre, *J. Amer. Chem. Soc.*, 1954, **76**, 3240; Long and Paul, *Chem. Rev.* 1957, **57**, 935.
[20] Gold and Satchell, *J.*, 1955, 2743, 3619, 3622.
[21] Satchell, *J.*, 1956, 3911.
[22] Gold and Hilton, *J.*, 1955, 843.

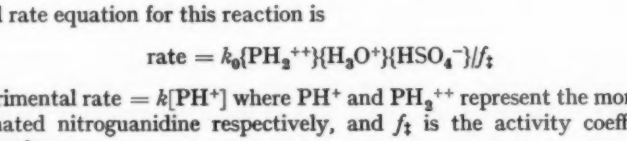
acid. It may be significant that this medium is very close to that corresponding to the 1 : 1 mole ratio of sulphuric acid to water and possibly a change of mechanism occurs at the higher acidities. As the results in Table 1 show, the sum of the terms log $\{H_2SO_4\}$ + log $\{H_2O\}$ increases continuously with acidity as does that of the terms log k and H_0. It is the difference between these two sets of values which remains constant. The constancy of the terms in equation (2) is consistent with a rate constant represented by equation (3)

$$k = \text{constant}\ \{H_2SO_4\}\ \{H^+\}\ \{H_2O\}\ f_B/f_{BH^+} \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and this in turn implies a transition complex formed from a nitroguanidine cation PH^+ and the solvent species H_3O^+ and H_2SO_4. If molecular sulphuric acid is absent from the more aqueous sulphuric acid solutions used for denitration, the same transition complex could equally well be formed from the diprotonated nitroguanidine PH_2^{++} and the solvent species HSO_4^- and H_3O^+, both of which should be present in excess in most, if not all, of the media studied. The absorption spectra indicate that addition of a proton to nitroguanidine occurs at the nitrimino-nitrogen atom (see following paper). Denitration of this ion would lead to the formation of a guanidinium ion and a nitronium ion, a process which requires an additional proton

$$(NH_2)_2C{=}\overset{+}{N}HNO_2 + H^+ \rightleftharpoons (NH_2)_2C{=}\overset{+}{N}H_2 + NO_2^+$$

The proton will be supplied by either of the acid species present, H_3O^+ or H_2SO_4, but bimolecular reaction of either with the nitroguanidinium ion can be excluded, as the previously reported failure [1] of the experimental results to conform to a bimolecular mechanism of this type was confirmed for all compounds now studied. If the additional proton becomes attached to the nitroguanidinium ion in any initial fast step, it will almost certainly be located on one of the two amino-groups and the denitration of the bivalent ion so formed through a transition complex which includes a bisulphate and oxonium ion could be represented as shown



The Brönsted rate equation for this reaction is

$$\text{rate} = k_0\{PH_2^{++}\}\{H_3O^+\}\{HSO_4^-\}/f_\ddagger$$

and the experimental rate $= k[PH^+]$ where PH^+ and PH_2^{++} represent the monoprotonated and diprotonated nitroguanidine respectively, and $f_\ddagger$ is the activity coefficient of the transition complex:

$$k = k_0\{PH_2^{++}\}\{H_3O^+\}\{HSO_4^-\}/[Ph^+]f_\ddagger$$

From the equilibria $H_2O + H_2SO_4 \rightleftharpoons H_3O^+ + HSO_4^-$; $PH^+ + H^+ \rightleftharpoons PH_2^{++}$ which have the thermodynamic equilibrium constants K_{H_2O} and $K_{PH_2^{++}}$, respectively, we have

$$k = k_0K_{PH_2^{++}}K_{H_2O}\{H^+\}\{H_2O\}\{H_2SO_4\}f_{PH^+}/f_\ddagger$$

and since $$H_0 = -\log\{H^+\}f_B/f_{BH^+}$$

$$\log k = \log k_0K_{PH_2^{++}}K_{H_2O} - H_0 + \log\{H_2O\} + \log\{H_2SO_4\} + \log f_{PH^+}f_{BH^+}/f_Bf_\ddagger$$

which agrees with the empirical equation 2 if the activity coefficient term remains constant.

The range of media in which this combination of reactant and solvent species could be expected to be formed most readily is from that of the 1 : 1 molar ratio of water to sulphuric acid (84·5%) to that of the 2 : 1 molar ratio (72·5%) since within this range it is probable that H_3O^+ is the strongest proton donator and HSO_4^- the strongest proton acceptor. This range largely coincides with that found experimentally for the application of equation 2.

The aqueous perchloric acid used corresponds in acidity to the aqueous sulphuric acid range below the 2 : 1 molar ratio of water to sulphuric acid. While H_3O^+ is the strongest acid present, there is no base equivalent to the HSO_4^- ion in aqueous perchloric acid and this may be the reason for the slower reaction and the operation of a different mechanism of denitration with the rate depending mainly on the acidity.

Effect of Change of the Initial Concentration of Reactant on the Rate Constant.—The slight decrease in the rate constant of denitration with increase in initial concentration of the nitroguanidine previously [1,3] observed was confirmed for 2-nitrimino-1 : 3-diaza*cyclo*hexane and *NN*-dimethyl-*N'*-nitroguanidine but the effect was dependent on the particular medium in which the rates were measured. In more aqueous media the effect was virtually eliminated. The rate constant for 2-nitrimino-1 : 3-diaza*cyclo*pentane was independent of initial concentration of reactant over a twenty-fold range from $4{\cdot}5 \times 10^{-3}$ to 10^{-1} mole/l.; a similar result was found for the 4-methyl analogue. No conclusion has been reached on this difference in behaviour of nitroguanidines.

The Extent of Denitration at Equilibrium.—Although rates of denitration become immeasurably fast above 90% sulphuric acid for all but one of the compounds in Table 1, data on the equilibria attained in all media up to *ca.* 95% sulphuric acid were obtained by determining the equilibrium concentration of the nitroguanidine spectroscopically. Equilibrium concentrations were also measured for the denitration of the diaza*cyclo*hexane and of *N*-methyl-*N'*-nitroguanidine in perchloric acid and for the same equilibrium attained by guanidine nitrate in sulphuric acid–acetic acid. The variation in the extent of denitration in aqueous sulphuric acid with medium composition is shown in Fig. 2; a minimum for all compounds occurs at 85—88% sulphuric acid. With sulphuric acid–acetic acid there is a similar minimum at 73% sulphuric acid. In both sulphuric acid–water and sulphuric acid–acetic acid, the composition of the media where the minimum occurs is such that the mole ratio of sulphuric acid to the other component is greater than 1 but in the strongest perchloric acid used (72%) this ratio is much less than 1. A minimum is therefore not observed in the latter because a sufficiently high mole ratio of acid to water cannot be attained.

Since the percentage denitration is a measure of the ratio of the rate of denitration to rate of nitration, it is evident that as the acid strength increases, the rate of nitration at first increases more rapidly than that of denitration, but as the point of minimum denitration is approached this difference is not maintained. The rate of denitration increases sharply above this point as the results for 2-nitrimino-1 : 3-diaza*cyclo*pentane (Table 1) indicate; if the nitration shows the same phenomenon of attaining a maximum rate in *ca.* 90% sulphuric acid as already established for aromatic nitration [23] the occurrence of a minimum is to be expected. The corresponding maximum amount of nitration has been found in the equilibria attained in the nitration of tetraethylguanidine in sulphuric acid, the maximum occurring when the water content of the medium is 10—15%.[24]

A relation between the equilibrium constant and the activity of water has been adduced by Simkins and Williams,[2] given by

$$\log K_0 = \log K + \log \{H_2O\} + \log (f_{PH^+}/f_{GH^+} f_{HNO_3})$$

where K_0 represents a thermodynamic equilibrium constant, K the ratio of equilibrium concentrations $[PH^+]/[GH^+][HNO_3]$, $\{H_2O\}$ the activity of water, and f_{PH^+}, f_{GH^+}, and f_{HNO_3} the activity coefficient of the nitroguanidine ion, the guanidinium ion, and nitric acid, respectively. This has been tested by plotting log k against log $\{H_2O\}$, for sulphuric acid–water (the only medium for which the necessary data are available). With 2-nitrimino-1 : 3-diaza*cyclo*hexane and *NN*-dimethyl-*N'*-nitroguanidine good straight lines were obtained for media up to that corresponding to minimum denitration with slopes of −0·99 and −1·23, respectively. 2-Nitrimino-1 : 3-4-triazole gives an initial

[23] Bonner, James, Lowen, and Williams, *Nature*, 1949, **163**, 955.
[24] Kirkwood and Wright, *Canad. J. Chem.*, 1957, **35**, 527.

straight-line plot of slope −0·90, but this falls off rapidly above 80% sulphuric acid. For 2-nitrimino-1 : 3-diaza*cyclo*pentane and its 4-methyl derivative, the extent of denitration is more than 80% in most media, and the back reaction occurs to such a slight extent that it is not possible to deduce reliable values for K.

Rates, k_2, of the nitration can be calculated from the equilibrium constant K and the rate of the forward reaction k, since $K = k_2/k_1$. Reliable values are only possible for 2-nitramino-1 : 3 : 4-triazole, 2-nitrimino-1 : 3-diaza*cyclo*hexane, and *NN*-dimethyl-*N'*-nitroguanidine since the equilibrium is displaced too far in favour of the forward reaction for the other two compounds in Table 1.

Comparison of the rates of nitration for these three compounds with the acidity function J_0 [25] confirms that nitration of guanidines occurs through the nitronium ion; in each case log k_2 is a linear function of J_0 with slope approximately as indicated: 2-amino-1 : 3 : 4-triazole (0·97), 2-imino-1 : 3-diaza*cyclo*hexane (0·83), and *NN'*-dimethylguanidine (0·94).

Some attempt was made to measure the rate of nitration of guanidine in sulphuric acid–acetic acid but although preliminary results suggest 99% conversion of the guanidine, substantial decomposition to products other than nitroguanidine was evident, and further investigation of these side-reactions is necessary.

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[25] Williams and Bevan, *Chem. and Ind.*, 1955, 171.

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784. *The Denitration of Nitroguanidines in Strong Acids. Part II.* Absorption Spectra and* pK_a *Values of Certain Nitroguanidines.*

By T. G. BONNER and J. C. LOCKHART.

The structure of certain nitroguanidines and their conjugate acids is discussed and ultraviolet absorption spectra data are adduced to support the nitrimino-form of the free base and the nitramino-form for the ion. Differences in absorption spectra and basicity of the nitroguanidines investigated are interpreted in terms of the resonance structures of the free bases and their conjugate acids.

SOME controversy has existed over the structure of nitroguanidine, the choice being between two tautomers, the nitramino-form (Ia) and the nitrimino-form (Ib).

$NH{:}C(NH_2){\cdot}NH{\cdot}NO_2$ (Ia) $\qquad$ $NH_2{\cdot}C(NH_2){:}N{\cdot}NO_2$ (Ib)

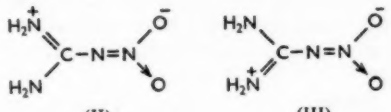
Wright [1] favoured structure (Ib) since no reaction occurs between nitroguanidine and diazomethane or acetyl chloride, both of which react readily with nitramines; the same is true of 2-nitrimino-1 : 3-diaza*cyclo*pentane. Other evidence for the nitrimino-structure comes from dipole-moment measurements [2] but absorption spectra have been interpreted as evidence for both forms.[2,3]

An *X*-ray study [4] of nitroguanidine showed the molecule to be almost planar with the carbon atom practically equidistant from the three nitrogen atoms to which it is directly attached. This implies that all three carbon–nitrogen bonds have the same bond order,

* Part I, preceding paper.

[1] Kirkwood and Wright, *J. Org. Chem.*, 1953, **18**, 629.
[2] Kumler and Sah, *ibid.*, p. 669.
[3] McKay, Picard, and Brunet, *Canad. J. Chem.*, 1951, **29**, 746.
[4] Bryden, Burkardt, Hughes, and Donohue, *Acta Cryst.*, 1956, **9**, 573.

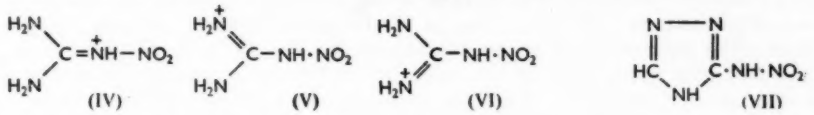
which is not consistent with either form (Ia) or (Ib). The authors have represented the molecule by eight resonance structures of which the positions of the nuclei are those of the nitrimino-form (Ib), and an attempt was made to weight these structures so that a symmetrical electron distribution exists around the carbon atom. However, equal contributions from the covalent structure (Ib) and the ionic structures (II) and (III) would produce the symmetry found.



(II) (III)

Recent evidence for the nitramino-structure has been provided by an investigation by proton magnetic resonance of nitroguanidine.[5] The curve obtained does not give any indication of the two single protons present in structure (Ia) and is characteristic of proton pairs only, in accordance with structure (Ib).

This conclusion is now confirmed by the ultraviolet absorption spectra of nitroguanidine and its conjugate acid which, although previously investigated, have now been more extensively studied together with several derivatives. In all these nitroguanidines the existence of a strong absorption band at 2600—2700 Å has been observed, the exact position and intensity of which depends on the substituent groups. The absorption spectrum of nitramide [6] is quite different with a broad band at 2250 Å (ε 5900; in water), which suggests that nitroguanidines do not exist in the nitramino-form (Ia). The absorption band characteristic of nitramide appears in the spectra of nitroguanidines in strongly acid solution and reaches maximum intensity in 40—50% sulphuric acid corresponding to complete conversion of the nitroguanidine into its conjugate acid. The change is accompanied by the disappearance of the absorption band characteristic of the free base. A typical example of this change is that of 2-nitrimino-1 : 3-diaza*cyclo*pentane shown in Fig. 1. A nitramino-structure would be readily acquired by the conjugate acid by proton uptake on the nitrimino-nitrogen atom. Three principal resonance structures (IV)—(VI) can represent the nitroguanidinium ion thus formed.



(IV) (V) (VI) (VII)

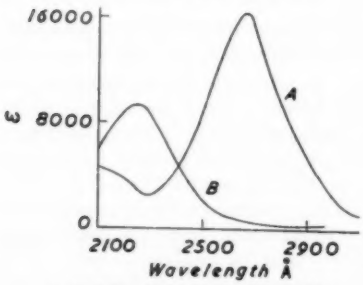
As shown in the Table, the majority of nitroguanidine derivatives undergo this characteristic change of spectrum on conversion into their conjugate acids in sulphuric acid. The only exception is 2-nitramino-1 : 3 : 4-triazole, which shows the same hypsochromic shift but to a lesser extent. Evidently the triazole has structural features which modify its absorption characteristics. An aromatic structure for the triazole ring requires the nitramino-form (VII) and the characteristic spectrum of nitramine will be modified by conjugation of the nitramino-group with the ring. Protonation in strongly acid solution will occur at one of the nitrogen atoms, probably at either of the tertiary atoms, and this will reduce conjugation of the nitramino-group with the ring but not sufficiently to produce the spectrum of nitramine.

The lower extinction coefficient of *NN*-dimethyl-*N'*-nitroguanidine is clearly an example of steric inhibition of conjugation. If the transition corresponding to the intense absorption of nitroguanidine bases at 2600—2700 Å is from the homopolar ground state (Ib) to the predominantly dipolar excited state (II), the presence of two methyl groups

[5] Richards and Yorke, *Trans. Faraday Soc.*, 1958, **54**, 321
[6] Jones and Thorn, *Canad. J. Res.*, 1949, **B27**, 828.

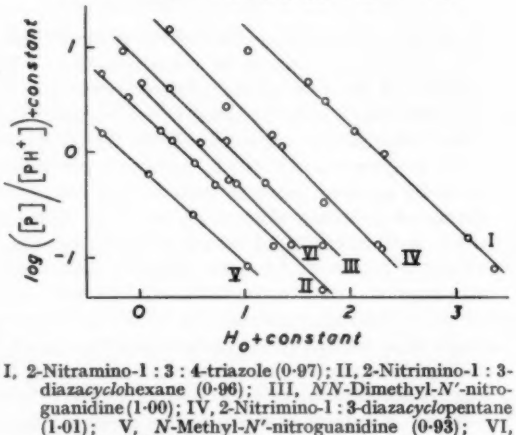
on one amino-nitrogen atom will restrict rotation about the bond linking this nitrogen atom to the central carbon atom and hinder the molecule's attaining the planar configuration necessary for maximum resonance. As the intensity of absorption only is reduced, $\lambda_{max.}$ remaining unchanged, the steric hindrance is relatively weak and is possibly associated with transitions between non-planar ground state and near-planar excited states.[7] The relatively smaller fall in intensity of the symmetrical *NN'*-dimethyl-*N''*-nitroguanidine may be the result of a weaker operation of this effect. The greatest intensity of absorption occurs in the diaza*cyclo*pentane and diaza*cyclo*hexane derivatives, and this can be attributed to the rigidity of these ring systems facilitating the formation of the planar configuration of the dipolar excited state.

FIG. 1. *Spectrum of* 2-*nitrimino*-1 : 3-*diaza*-cyclo*pentane in sulphuric acid.*



A, in 0·1N-acid; *B*, in 69% acid.

FIG. 2. *Variation of log* ([P]/[PH⁺]) *with* H_0.



I, 2-Nitramino-1 : 3 : 4-triazole (0·97); II, 2-Nitrimino-1 : 3-diaza*cyclo*hexane (0·96); III, *NN*-Dimethyl-*N'*-nitroguanidine (1·00); IV, 2-Nitrimino-1 : 3-diaza*cyclo*pentane (1·01); V, *N*-Methyl-*N'*-nitroguanidine (0·93); VI, Nitroguanidine (1·02).

Values in parentheses are of log ([P]/[PH⁺])/H_0.

pK_a *Values of Nitroguanidines.*—pK_a values are given in the Table. As the absorption spectra of the nitroguanidium ions (except the triazole derivative) indicate a nitramino-structure (IV) corresponding to proton uptake on the nitrimino-nitrogen atom, the relative basicities will depend on the resonance stabilisation achieved by contributions from structures (V) and (VI). The slight increase in basicity (pK_a increases from −0·93 to −0·86) produced by the introduction of a single methyl group on the amino-nitrogen atom is in accord with the inductive effect of this group but the considerable decrease in basicity which follows the substitution of a second methyl group on the same nitrogen atom (pK_a = −1·20) is evidence of the greater strain involved in attaining the planar configuration necessary for appreciable contributions in the ground state from the resonance structures of the type (V).

The markedly higher basicity of the diaza*cyclo*hexane (pK_a = −0·71) than of the diaza*cyclo*pentane (pK_a = −1·36) can be related to the relative stability of these ring systems with respect to the exocyclic double bond. Since a double bond which is exocyclic to a five-membered ring is more stable than one which is exocyclic to a six-membered ring,[8] it is possible that greater contributions to the resonance stabilisation from the equivalent structures corresponding to (V) and (VI) will be made in the case of the conjugate acid of the diaza*cyclo*hexane than in that of the diaza*cyclo*pentane.

The notably weak basic character of 2-nitramino-1 : 3 : 4-triazole is characteristic

[7] Braude and Waight, "Progress in Stereochemistry," ed. Klyne, Butterworths, London, 1954, p. 126; Baddeley, *Ann. Reports*, 1955, **52**, 131.

[8] Fleck, *J. Org. Chem.*, 1957, **22**, 439; Brown, *ibid.*, p. 439.

Absorption spectra data, pK_a values, and relative rates (RR) of denitration, in aqueous sulphuric acid.

Compound	Free base		Conjugate acid			
	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	pK_a	*RR*
2-Nitramino-1 : 3 : 4-triazole	12,400	2820	6700	2470	−2·5	16·6
2-Nitrimino-1 : 3-diaza*cyclo*hexane	15,450	2680	9700	2315	−0·71	8·5
NN-Dimethyl-*N'*-nitroguanidine	11,350	2710	8010	2250	−1·30	6·6
NN'-Dimethyl-*N''*-nitroguanidine	13,200	2675	—	—	—	6·3 [a]
N-Methyl-*N'*-nitroguanidine	14,040	2670	8700	2260	−0·86	3·8 [a]
Nitroguanidine	14,400	2640	9940	2250	−0·93 [b]	1 [c]
4-Methyl-2-nitrimino-1 : 3-diaza*cyclo*pentane	17,140	2660	—	—	—	0·41
2-Nitrimino-1 : 3-diaza*cyclo*pentane	16,170	2655	9440	2260	−1·36	0·33

[a] Ref. 9. [b] The pK_a obtained for nitroguanidine above agrees with that obtained in dilute hydrochloric acid,[11] recalculated on an H_0 basis. [c] Ref. 10.

of aromatic bases (cf. aniline, pyridine) and originates in the decrease in resonance which results from proton addition to a nitrogen atom.

A significant feature of the ionisation of each nitroguanidine is that a plot of log ([P]/[PH$^+$]) (where P represents the uncharged nitroguanidine and PH$^+$ its conjugate acid) against H_0 is a straight line of slope 1, as shown in Fig. 2. These compounds are therefore indistinguishable in their ionisation behaviour from the aromatic bases used by Hammett in the evaluation of the H_0 scale.

Relative Rates of Denitration.—The mechanism of denitration of nitroguanidines in strong acids (previous paper) envisages the expulsion of a nitronium ion from the diprotonated base accompanied by proton transfer involving acid and base species present in the medium. An important factor in this process is the ease of proton uptake, with the second protonation more important than the first. Thus although the triazole is the weakest base, its conjugate acid has the largest number of basic centres for the second protonation, and if this second protonation occurs more readily than with the other nitroguanidinium ions, the relatively high rate of nitration found experimentally would be expected. The order of denitration rates for nitroguanidine and its monomethyl and dimethyl derivatives is also in accord with the expected basicity of their conjugate acids, if this is assumed to depend mainly on the inductive effect on the methyl group. The difference in rates of denitration of the diaza*cyclo*hexane derivative and its *cyclo*pentane analogue may be attributed to differences in ring stability, the faster rate for the former corresponding to a greater flexibility of the six-membered ring compared with the five-membered ring in the diprotonated derivatives (the second proton being assumed to add to a ring nitrogen atom).

Experimental

Materials.—These were as in the preceding paper.

Absorption Spectra.—These were measured on a Hilger Uvispek spectrophotometer calibrated with potassium chromate.[12]

Measurement of Ionisation Ratios.—The method developed by Flexser, Hammett, and Dingwall [13] was used. Indicator ionisation ratios were obtained from the equation $[B]/[BH^+] = (\varepsilon_{BH^+} - \varepsilon)/(\varepsilon - \varepsilon_B)$, where ε_B and ε_{BH^+} are the extinction coefficients of the un-ionised base B and its conjugate acid BH^+ at any selected wavelength and ε is that of the mixture of the same wavelength. pK_a values were obtained from the relation $pK_a = H_0 - \log([B]/[BH^+])$, where [B] and [$BH^+$] are the concentrations of the base and its conjugate acid in a medium of acidity H_0. The results recorded in the Table are the mean of several values obtained at different H_0 values and different wavelengths.

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[*Received, May 1st,* 1958.]

[9] Hardy-Klein, *J.*, 1957, 70.
[10] Simkins and Williams, *J.*, 1952, 3086.
[11] Hall, de Vries, and St. Clair Gantz, *J. Amer. Chem. Soc.*, 1955, **77**, 6507.
[12] Hogness, Zscheile, and Sidwell, *J. Phys. Chem.*, 1937, **41**, 379.
[13] Flexser, Hammett, and Dingwall, *J. Amer. Chem. Soc.*, 1935, **57**, 2103.

785. *Polysaccharides of Baker's Yeast. Part II.* Yeast Glucan.*

By Stanley Peat, W. J. Whelan, and T. E. Edwards.

Baker's yeast glucan has been partly hydrolysed with acid, and the products have been fractionated on charcoal–Celite. Eight mono-, di-, tri-, and tetra-saccharides, considered to be fragments of the glucan molecule, have been isolated and identified. These are D-glucose, gentiobiose, laminaribiose, gentiotriose, 6-*O*-β-laminaribiosylglucose, laminaritriose, 3-*O*-β-gentiobiosylglucose, and gentiotetraose. It is concluded that the glucan is a linear polymer of β-D-glucopyranose in which 1 : 3- and 1 : 6-linkages are arranged at random or in sequences such that a group of at least three 1 : 6-linkages is flanked on either side by 1 : 3-linkages. Periodate-oxidation results suggest that the combined proportion of non-reducing end groups and 1 : 6-links is 1 per 10 glucose residues.

Baker's yeast contains a cell-wall polysaccharide (yeast glucan) which " can be isolated free from other material, still retaining the shape of the whole cell and obviously constituting a complete membrane." [1] The original name " yeast cellulose," applied by Salkowski,[2] reflects the insolubility and inert character of this substance. The polysaccharide was distinguished from cellulose by Zechmeister and Toth,[3] who showed that it did not give the colour reactions of cellulose but that it was, nevertheless, a polyglucose since the major product of hydrolysis of the methylated glucan was 2 : 4 : 6-tri-*O*-methyl-D-glucose. The same result was obtained by Hassid, Joslyn, and McCready.[4] In neither case was tetra-*O*-methylglucose detected. The main polymeric linkage is therefore of the 1 : 3-type and the low specific optical rotations of the acetyl and the methyl derivatives of the glucan suggest that the glucose units are in the β-form. Barry and Dillon [5] found that the glucan was oxidised to only a small extent by periodate and isolated laminaribiose (as the osazone) from a hydrolysate of the oxidised polysaccharide, confirming the conception of β-1 : 3-linkages. From a study of yeast glucan by methylation and periodate oxidation Bell and Northcote [6] concluded that this polyglucose is a highly branched structure in which unit chains of about nine 1 : 3-linked β-glucose radicals are interconnected through 1 : 2-links. These workers report a substantial yield of tetra-*O*-methylglucose (about 10%, molar basis) from the methylated glucan.

We have investigated the glucan by partial hydrolysis and examination of the oligosaccharide fragments, as for yeast glycogen.[7] The glucan was isolated, following the method of Bell and Northcote,[6] by extracting baker's yeast with alkali to remove mannan and then with dilute acetic acid to remove glycogen. We found the latter treatment not to be fully effective, but complete extraction of glycogen was achieved by autoclaving. The vacuum-dried (60°) glucan contained polyglucose (90·3%), ash (0·4%), and nitrogen (0·6%). The tri-*O*-acetyl derivative had the specific optical rotation (−62·3°) recorded by Bell and Northcote.[6]

It proved impossible appreciably to hydrolyse the polysaccharide in hot 0·33N-sulphuric acid, and acetolysis proceeded only very slowly (9% degradation in 93 hr.). The glucan was, however, soluble in hot 90% formic acid and was submitted to hydrolysis in this solvent until it became soluble in dilute sulphuric acid, heating in which caused further hydrolysis and elimination of the formyl esters produced in the first stage.[8] A partial

* Part I, *J.*, 1955, 355.

[1] Northcote and Horne, *Biochem. J.*, 1952, **51**, 232.
[2] Salkowski, *Ber.*, 1894, **27**, 3325; *Z. physiol. Chem.*, 1914, **92**, 75.
[3] Zechmeister and Toth, *Biochem. Z.*, 1934, **270**, 309; 1936, **284**, 133.
[4] Hassid, Josyln, and McCready, *J. Amer. Chem. Soc.*, 1941, **63**, 295.
[5] Barry and Dillon, *Proc. Roy. Irish Acad.*, 1943, **49**, *B*, 177.
[6] Bell and Northcote, *J.*, 1950, 1944.
[7] Peat, Whelan, and Edwards, *J.*, 1955, 355.
[8] Andrews, Hough, and Jones, *J.*, 1953, 1186.

acid hydrolysate [40·6% apparent conversion of the polysaccharide (25·4 g.) into glucose] was then fractionated on charcoal–Celite.[9-11] The fractions were combined in batches and examined by paper chromatography and ionophoresis. When necessary, further fractionation was effected by preparative-scale paper chromatography. In most cases the sugars were characterised by measurement of specific optical rotation and by the preparations of the crystalline β-acetyl derivatives. The yields and properties of the mono- and oligo-saccharides isolated are shown in the Table.

Physical properties of the partial hydrolysis products of yeast glucan.

Sugar *	Source †	Yield ‡ (g.)	$[\alpha]_D$ in water	β-Acetate M. p.	β-Acetate $[\alpha]_D$ in $CHCl_3$
Glucose	G	*ca.* 6·0	—	131°	—
	A	—	—	131	—
Gentiobiose	G	0·473	+11·5°	192—193	−5·1°
	A	—	+9·9	191—192	−5·3
Laminaribiose	G	3·17	+20·5	162—163	−28·1
	A	—	+18·6	160—161	−28·8
Gentiotriose	G	0·159	−10·5	212—213	−7·7
	A	—	−10·3	214—215	−9·4
6-*O*-β-Laminaribiosylglucose	G	0·137	—	215—216	−25·0
	A	—	—	217—218	−27·0
Laminaritriose	G	1·17	+2·2	121	−40·3
	A	—	+2·3	120—121	−40·4
3-*O*-β-Gentiobiosylglucose	G	0·100	—	—	—
Gentiotetraose	G	0·168	−15·9	—	—
	A	—	−18·4	—	—

* Di- and tri-saccharides are listed in the order in which they emerged from the charcoal–Celite column.

† G = glucan, A = authentic specimen.

‡ From 30 g. of air-dried glucan, containing 25·4 g. of polyglucose, hydrolysed to 40·6% apparent conversion into glucose.

Mono- and Di-saccharide Products of Hydrolysis.—The only monosaccharide detected was glucose. There was no evidence of the presence of mannitol (found in the β-1 : 3-linked glucose polymer, laminarin [12,13]). It was expected from the work of Bell and Northcote [6] that the disaccharide products would be laminaribiose and sophorose [*O*-β-D-glucopyranosyl-(1 ⟶ 2)-D-glucose]. Laminaribiose was obtained in quantity (3·17 g. from 30 g.) and a second disaccharide was present. The latter proved to be, not sophorose, but gentiobiose (473 mg.). Circumstantial evidence was obtained of the presence of a very small amount of isomaltose (21 mg.) (see p. 3867) but since a greater quantity (50 mg.) was isolated when glucose (21·3 g.) was similarly treated with formic and sulphuric acids [14] it was concluded that the isomaltose was a reversion product. The weight (52 mg.) of gentiobiose formed during acid reversion [14] was much less than was isolated from the glucan. The laminaribiose and gentiobiose were characterised as shown in the Table and the gentiobiose was also oxidised with sodium metaperiodate; 4·7 molecular proportions of formic acid were released (Calc. for gentiobiose: 5 mol. prop.).

Tri- and Tetra-saccharide Products of Hydrolysis.—Four trisaccharides were isolated and three were identified as the crystalline acetates (see Table). In order of elution from the charcoal column, these were gentiotriose, 6-*O*-β-laminaribiosylglucose, laminaritriose, and 3-*O*-β-gentiobiosylglucose. The last three oligosaccharides had also been obtained from insoluble laminarin.[13] Gentiotriose and laminaritriose were identified by comparison with authentic specimens of these trisaccharides. In the case of the two "mixed" trisaccharides (those containing 1 : 3- and 1 : 6-linkages) the authentic compounds had

[9] Whistler and Durso, *J. Amer. Chem. Soc.*, 1950, **72**, 677.
[10] Whelan, Bailey, and Roberts, *J.*, 1953, 1293.
[11] Alm, *Acta Chem. Scand.*, 1952, **6**, 1186.
[12] Peat, Whelan, and Lawley, *Chem. and Ind.*, 1955, 35.
[13] *Idem*, *J.*, 1958, **724**, 729.
[14] Peat, Whelan, Edwards, and Owen, *J.*, 1958, 586.

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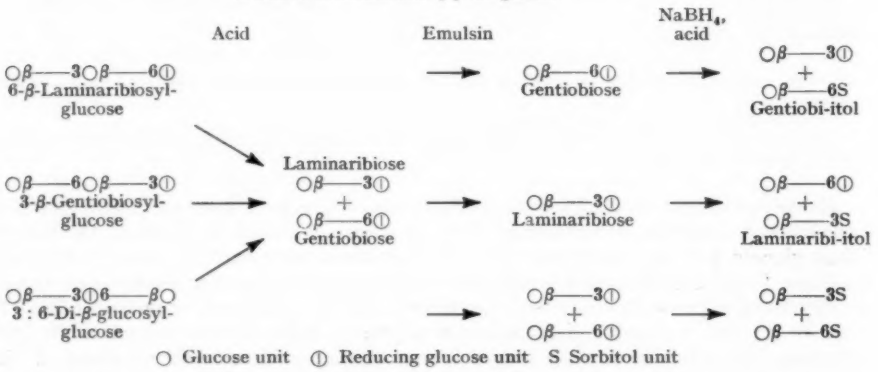
been prepared by chemical synthesis and were used to study the mode of action of the β-glucosidase of sweet almonds (emulsin).[15] 6-*O*-β-Laminaribiosylglucose, hydrolysed by this enzyme, yields gentiobiose, but not laminaribiose, as an intermediate product, whereas 3-*O*-β-gentiobiosylglucose gives laminaribiose, but not gentiobiose. It is clear that this β-glucosidase acts by removing the non-reducing end glucose unit and that it cannot hydrolyse the reducing-end linkage in either of these trisaccharides.

The evidence of identification of the two " mixed-linkage " trisaccharide is as follows. The first to be eluted gave gentiobiose and laminaribiose as the products of partial acid hydrolysis. Emulsin released gentiobiose, but not laminaribiose. After reduction of the trisaccharide with borohydride and partial hydrolysis, the " disaccharide " products were laminaribiose and a non-reducing compound which had the R_F value of gentiobi-itol. These observations establish the structure of the trisaccharide as 6-*O*-β-laminaribiosylglucose (Fig. 1). Confirmatory evidence came from the comparison of the crystalline acetate with that of the chemically synthesised trisaccharide (see Table). Partial acid hydrolysis of the second trisaccharide also gave gentiobiose and laminaribiose; emulsin liberated laminaribiose, and the borohydride-reduced trisaccharide gave gentiobiose as the only reducing disaccharide in the partial acid hydrolysate. The trisaccharide is therefore

FIG. 1. *Disaccharide products of the partial acid and enzymic hydrolysis of some of the possible structural trisaccharides of yeast glucan.*



3-*O*-β-gentiobiosylglucose (Fig. 1). Its R_F value was identical with that of the authentic specimen. There was no evidence of the presence in any fraction of 3 : 6-di-*O*-β-glucosylglucose (see Fig. 1). Only one tetrasaccharide was separated in a form sufficiently pure to be identified. This was gentiotetraose.

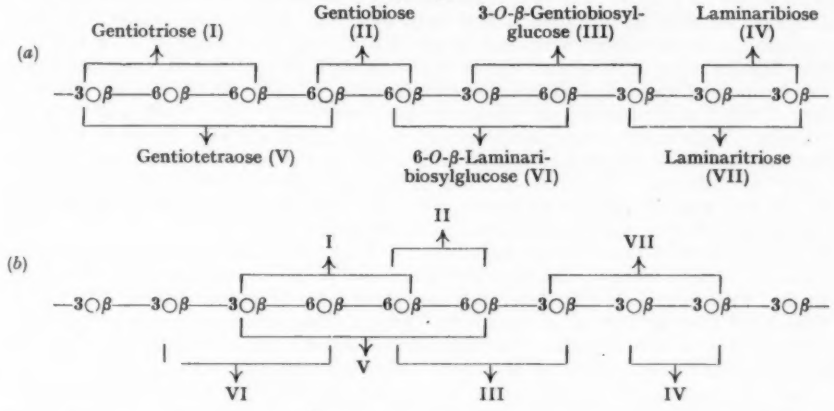
Structure of Yeast Glucan.—The foregoing evidence permits of the following conclusions. (i) Yeast glucan is constituted of β-glucopyranose units. (ii) While the majority of the glucose units are jointed by 1 : 3-linkages, there is a small proportion of 1 : 6-links. (iii) Having regard to the apparent absence of 3 : 6-di-*O*-β-glucosylglucose from the hydrolysis products, the glucan molecule is probably unbranched. (iv) The isolation of 3-*O*-β-gentiobiosylglucose and 6-*O*-β-laminaribiosylglucose shows that the two types of linkage occur in the same molecule. (v) The four trisaccharides isolated (see Table) are just those to be expected from a linear molecule containing a random arrangement of the linkages. This is shown in Fig. 2*a*. Alternatively, a " block " of 1 : 6-linked glucose units flanked on either side by 1 : 3-linked units would also satisfy the experimental findings (Fig. 2*b*): it is not possible to decide between the two types of structure on the evidence available.

The structure now proposed for yeast glucan is very different from that proposed by

[15] Peat, Whelan, and Evans, unpublished work.

Bell and Northcote,[6] both as to the nature of the minor linkage and the shape of the molecule. We have found no evidence for the presence of the 1 : 2-linkages inferred by Bell and Northcote from the isolation of 4 : 6-di-*O*-methylglucose from the methylated and hydrolysed polysaccharide. On the other hand, we have confirmed the presence of 1 : 6-links in yeast glucan by an alternative method which is described in the succeeding paper.[16]

FIG. 2. *Alternative structures of yeast glucan, showing the origin of the identified products of partial hydrolysis.*



Bell and Northcote " accounted for *ca.* 10% of the original polysaccharide " in the form of 2 : 3 : 4 : 6-tetra-, 2 : 4 : 6-tri-, and 4 : 6-di-*O*-methylglucose, in the molar ratio 1 : 7 : 1. Deductions as to structure based upon this ratio would be valid only if the polysaccharide were fully methylated. The actual methoxyl content, was, however, 41·7%, the calculated value for a tri-*O*-methylpolyglucose being 45·6%.

Bell and Northcote [6] found that oxidation of the glucan with metaperiodate liberated 1 molecular proportion of formic acid per 10·2 glucose residues. It was assumed that this acid was derived exclusively from the non-reducing end groups and the assumption seemed justified since the proportion of non-reducing end groups measured by methylation analysis was 1 in 9 glucose residues. However, a 1 : 6-linked glucose residue, such as we believe to be present in yeast glucan, contains the same 1 : 2 : 3-triol grouping, from which periodate liberates formic acid, as is present in a non-reducing end group. When oxidised with metaperiodate our specimen of glucan gave 1 molecule of acid per 10·3 glucose residues, but we regard this as a measure of the proportion of non-reducing end groups plus 1 : 6-linked glucose units, and not of end groups alone. It is assumed, as also by Bell and Northcote, that the reducing end groups of the glucan made a negligible contribution to the yield of acid, which was the amount present after the initial rapid oxidation had ceased. Reducing glucose end groups which are 3-linked are known not to yield acid at this stage, but 6-linked end glucose units yield 4 molecules of acid.[17] The initial oxidation was followed by a slower over-oxidation, characteristic of 3-linked but not of 6-linked end groups.[17] Some, if not all, of the reducing end groups were therefore 3-linked.

In the absence of knowledge of the molecular size of the glucan the periodate oxidation data cannot be used to estimate the proportion of 1 : 6-links but an approximation is given by the proportion of gentiobiose in the disaccharide fraction of the partial hydrolysate (13%; see Table). That at least three contiguous 1 : 6-links can occur in a yeast glucan chain is proved by the isolation of gentiotetraose from the partial hydrolysate but it is not

[16] Peat, Turvey, and Evans, succeeding paper.
[17] Lawley, Ph.D. Thesis, University of Wales, 1955.

known whether all the molecules are alike in this respect or whether the proportion and/or the arrangement of 1 : 6-links varies between individual molecules.

Experimental

General Methods.—These are described by Peat, Whelan, and Roberts [18] and in Part I of this series.[7] Solutions for optical rotations were in a 4 dm. tube. Small quantities (10 mg.) of sugar were reduced by treating them with an equal weight of sodium borohydride in about 1 ml. of solution for 2 hr. at room temperature. Excess of borohydride was then destroyed by the dropwise addition of 6N-sulphuric acid until evolution of hydrogen ceased. All paper-chromatographic fractionations were made in butan-1-ol–acetic acid–water (4 : 1 : 5, by vol.).

Periodate oxidation of the glucan was carried out exactly as by Bell and Northcote [6] except that the formic acid was measured by iodometric titration.[13] After 49, 96, 144, and 216 hr. the amounts of formic acid produced per glucose residue were 0·0875, 0·101, 0·106, and 0·112 mol., respectively. These results were plotted graphically and tangents were drawn to the curves representing the initial and secondary (over-oxidation) stages of oxidation, in order to determine the point of inflexion. This corresponded to an acid yield of 0·0972 mol. per glucose residue, or 10·3 glucose residues per molecule of acid. The measured carbohydrate content, and not the weight of the glucan, was used in calculating the results.

Isolation of Yeast Glucan.—Fresh baker's yeast (6 kg.; Distillers Co. Ltd.) was extracted with alkali (to remove mannan) and then with acetic acid (to remove glycogen).[6,7] The residue was washed with water in a centrifuge, then suspended in 0·02M-sodium acetate (pH 7·0; 2 l.) and heated for 1 hr. at 135° in an autoclave. After cooling, water (2 l.) was added and the residue separated in a centrifuge. The supernatant liquid gave an intense red colour with iodine, indicating the extraction of glycogen. After six washings of the residue with water (1·5 l. each) the wash-liquid was achroic but further autoclaving at 135° in 3 l. of water extracted more glycogen. The residue was therefore centrifuged, washed three times with water (2 l. each), and again autoclaved. This time the supernatant liquid was achroic. The gelatinous solid was dehydrated with ethanol (3 vol.), centrifuged, and washed successively with ethanol, ether, and light petroleum (b. p. 60—80°). The product (39 g.) was a light-buff-coloured powder. After being dried in a vacuum for 36 hr. at 60° over phosphoric oxide the glucan contained 0·4% of non-volatile matter and 0·6% of nitrogen. The carbohydrate content was measured by heating the dried material (75·2 mg.) with " AnalaR " 90% formic acid (5 ml.) in a boiling-water bath for 2 hr. After addition of 3N-sulphuric acid (20 ml.), the mixture was heated for 3 hr., then cooled, neutralised, and diluted to 50 ml. and the reducing power was measured, as for glucose.[19] When " AnalaR " glucose (55·3 mg.) was treated in the same way the recovery was 94·8%. After correction for this loss, the polyglucose content of the specimen was calculated to be 90·3%.

Acetylation of Yeast Glucan.—The method was that of Bell and Northcote.[6] The final product (451 mg. from 500 mg. of glucan) was dissolved in chloroform (300 mg. in 5 ml.) and precipitated with light petroleum (5 ml.; b. p. 40—60°). The precipitate had $[\alpha]_D$ −62·3° (*c* 0·58 in $CHCl_3$) (Found: $CH_3{\cdot}CO$, 45·3. Calc. for the tri-*O*-acetyl derivative: 44·8%).

Small-scale Hydrolysis of Glucan.—Yeast glucan (309 mg., containing 279 mg. of polyglucose) was heated at 100° with 90% formic acid (3·42 ml.) for 25 min. and then with a second portion of acid (1·14 ml.) for a further 15 min. Hot 0·44N-sulphuric acid (45·6 ml.) was then added and the resulting white suspension filtered through sintered glass. The filtrate was diluted to 50 ml. and heated in a boiling-water bath. Samples (2 ml.) were withdrawn at 30 min. intervals between 1 and 2·5 hr. These were cooled quickly and a 1 ml. portion neutralised, diluted to 25 ml. and used for measurement of reducing power (as glucose). After 1, 1·5, 2, and 2·5 hr. the percentage apparent conversions into glucose were 38·1, 59·3, 66·3, and 77·2, respectively.

Large-scale Hydrolysis and Fractionation of Glucan.—Air-dried glucan (*ca.* 30 g. containing 25·4 g. of polyglucose) was heated on a boiling-water bath with 90% formic acid (342 ml.) for 25 min. and for a further 15 min. with added acid (114 ml.). 0·44N-Sulphuric acid (4·56 l.) was added and heating continued for 1 hr. The reducing power of the partial hydrolysate corresponded to an apparent conversion into glucose of 40·6%. The neutralised hydrolysate was

[1] Peat, Whelan, and Roberts, *J.*, 1957, 3916.
[19] Somogyi, *J. Biol. Chem.*, 1945, **160**, 61.

filtered through sintered glass. The brown residue was washed with water, ethanol, and ether and dried to give a dark-brown solid (1·39 g.) having the elementary composition: C, 45·6; H, 7·08; N, 3·33; S, 1·00%. The filtrate was concentrated until the salts began to crystallise and then applied to a charcoal–Celite column [9, 10] (1 : 1 by wt.; 123 × 5·5 cm.). A 2 m. head of water was applied to the column and fractions (*ca.* 400 ml. each) were collected automatically. When the bulk of glucose had emerged (8·75 l. of eluate) an ethanol gradient [11] was applied to the column by feeding 30% ethanol through a constant-head device into 10 l. of water in a reservoir connected to the column. A further 19 l. of eluate were collected. The fractions were combined in batches of 7—10, evaporated, and examined by paper chromatography and ionophoresis.[17] All the oligosaccharide components had M_G values of 0·67.

Mono- and Di-saccharide Components of the Hydrolysate.—A portion of combined fractions No. 17—33 (585 mg.) was acetylated with sodium acetate–acetic anhydride and a chloroform-soluble syrup was obtained (792 mg., 63%) which yielded crystals from ethanol of glucose β-acetate (see Table).

Fractions No. 43—58 contained a single component which had the same R_F and M_G values as gentiobiose and isomaltose. The solid was dissolved in water (20 ml.), the mixture clarified with Somogyi's deproteinising reagents,[10, 20] and the supernatant liquid and washings were diluted to 50 ml. The amount of disaccharide, measured by acid hydrolysis to glucose,[21] was 319·4 mg. The sugar had $[\alpha]_D$ +17·2°. This value was consistent with the fraction's being a mixture of isomaltose ($[\alpha]_D$ +122°) and gentiobiose ($[\alpha]_D$ +9·6°) in the ratio 6·7 : 93·3. When a portion of the solution (5 ml.) was oxidised with 0·37M-sodium metaperiodate (5 ml.) at room temperature, production of formic acid ceased after 70 hr. and after 140 hr. corresponded to 4·7 mol. The remainder of the sugar solution was evaporated and acetylated, yielding a chloroform-soluble syrup (536 mg. from 280 mg. of sugar; 92%) from which β-gentiobiose octa-*O*-acetate was crystallised (see Table).

Fractions No. 59—73 (3·48 g., undried wt.) were shown by paper chromatography to contain gentiobiose and laminaribiose. A portion (600 mg.) was fractionated on 6 sheets of Whatman No. 3 paper and the two sugars were recovered quantitatively.[14] The amount of each sugar was determined by acid hydrolysis to glucose,[21] and the specific optical rotations were also measured (see Table). Analysis of the batch for sugar content showed it to contain 88·1% of disaccharide. These data were used to calculate the amounts of the two disaccharides in the batch. A portion of the laminaribiose (360 mg.) was acetylated and the chloroform-soluble syrup (750 mg., 100%) yielded a crystalline acetate (see Table). Fractions No. 74—81 (256 mg.) also gave the same acetate (m. p. 161°, $[\alpha]_D$ −29·3° in $CHCl_3$).

Identification of Gentiotriose.—Fractions No. 82—89 and 90—97 contained mainly gentiotriose and were combined and purified by chromatography on thick filter paper. Partial acid-hydrolysis followed by paper chromatographic fractionation yielded glucose, gentiobiose, and unchanged trisaccharide. After determination of $[\alpha]_D$ of the trisaccharide, the remaining material (159 mg.) was acetylated and the chloroform-soluble syrup (262 mg., 86%) deposited crystals of β-gentiotriose undeca-acetate from ethanol (see Table).

Identification of Gentiotetraose.—Fractions No. 98—107 (256 mg.) were fractionated on thick filter paper and three fractions were obtained: *A* (81·5 mg.), *B*, and *C* (51·4 mg.), R_F value increasing in that order. *B* had the R_F value of gentiotriose and was not examined further. Partial acid-hydrolysis of *A* liberated sugars having the same R_F values as glucose, gentiobiose, and gentiotriose. The R_M values of these last two sugars and that of *A* showed the linear relation between R_M and degree of polymerisation characteristic of a polymer-homologous series of sugars.[10, 22, 23] The tetrasaccharide *A* had $[\alpha]_D$ −15·9° in water (see Table).

Identification of 6-O-β-*Laminaribiosylglucose.*—A portion (1·36 g.) of fractions No. 108—116 (1·708 g.) was separated into three fractions by chromatography on thick filter paper. These were termed *D*, *E*, and *F*, in order of increasing R_F value. *E* had the same R_F value as *C*. When treated with emulsin both fractions *C* and *E* yielded gentiobiose and glucose. Partial acid-hydrolysis of *C* gave gentiobiose and laminaribiose as the disaccharide products. Fractions *C* and *E* were combined and a portion (8·4 mg.) was reduced with borohydride and thereafter partly hydrolysed with acid. The " disaccharide " components were laminaribiose

[20] Somogyi, *J. Biol. Chem.*, 1945, **160**, 69.
[21] Pirt and Whelan, *J. Sci. Food Agric.*, 1951, **2**, 224.
[22] Martin, Biochem. Soc. Symposium, 1950, No. 3, 4.
[23] French and Wild, *J. Amer. Chem. Soc.*, 1953, **75**, 2612.

and a non-reducing sugar having the same R_F value as gentiobi-itol (see Fig. 1). Acetylation of the mixed fraction *C* and *E* (50 mg.) gave a chloroform-soluble syrup (100 mg., 94%) from which crystals of β-6-*O*-β-laminaribiosylglucose undeca-acetate were obtained (see Table).

Identification of Laminaritriose.—Fraction *F* (see above) had the same R_F value as laminaritriose. The $[\alpha]_D$ of the sugar was measured and the crystalline β-acetate (1·03 g., 100%) was obtained from 512 mg. of sugar (see Table).

Identification of 3-O-β-*Gentiobiosylglucose.*—Fractions No. 124—131 (735 mg.) and No. 132—138 (170 mg.) contained laminaritriose and a sugar (*G*) migrating on paper between laminaritriose and -tetraose, and in the same position as authentic 3-*O*-β-gentiobiosylglucose.[15] The whole of fractions No. 132—138 and 600 mg. of fractions No. 124—131 were fractionated on thick filter paper to yield 137 mg. of *G*, still containing a little laminaritriose. Pure material (100 mg.) was obtained by repeating the fractionation. The disaccharide products of partial acid-hydrolysis of *G* were gentiobiose and laminaribiose; that of partial emulsin hydrolysis was laminaribiose only. The reduced trisaccharide gave rise to gentiobiose and laminaribi-itol when partly hydrolysed with acid (see Fig. 1).

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786. *Polysaccharides of Baker's Yeast. Part III.*[1] *The Presence of* 1 : 6-*Linkages in Yeast Glucan.*

By STANLEY PEAT, J. R. TURVEY, and J. M. EVANS.

The glucan from baker's yeast has been examined by the technique of toluene-*p*-sulphonylation followed by the replacement of primary tosyl groups by iodine. It is concluded from the iodine content of the product that some 10—20% of the primary hydroxyl groups are involved in 1 : 6-linkages. These results support the evidence given in Part II of this series.[1]

THE structure of the insoluble cell-wall polysaccharide from baker's yeast (yeast glucan) has been studied by methylation assay,[2-4] by periodate oxidation,[5] and more recently by partial acid hydrolysis and identification of the oligosaccharide fragments.[1] These investigations all lead to the conclusion that the predominant linkage in yeast glucan is β-1 : 3-glucosidic, but there is less certainty about the character of subsidiary linkages. Indeed methylation assay by earlier workers[2,3] appeared to show that no subsidiary linkages were present; on the other hand, Bell and Northcote, from the results of methylation assay and periodate oxidation, concluded that yeast glucan has a highly branched structure in which the branch linkage is 1 : 2-glucosidic[4] (see preceding paper). Peat, Whelan, and Edwards,[1] by examination of the products of partial acid hydrolysis, inferred a structure which is essentially unbranched and in which " blocks " of β-1 : 6-linked glucose units alternate with " blocks " of β-1 : 3-linked units. If it be assumed that the average chain is of such length that the formic acid derived, by periodate oxidation, from terminal groups may be neglected, then the 1 : 6-linkages constitute *ca.* 10% of the whole. In view of the dubiety involved in the methylation assay owing to incomplete methylation of the polysaccharide, and in the acid hydrolysis method owing to the possibility that some of the oligosaccharides isolated may be products of reversion synthesis, it was felt that independent methods for establishing the presence of other linkages were desirable in order to decide between the structures postulated. It is the purpose of this communication to describe the application of one such method to yeast glucan.

[1] Peat, Whelan, and Edwards, preceding paper.
[2] Zechmeister and Toth, *Biochem. Z.*, 1934, **270**, 309; 1936, **284**, 133.
[3] Hassid, Joslyn, and McCready, *J. Amer. Chem. Soc.*, 1941, **63**, 295.
[4] Bell and Northcote, *J.*, 1950, 1944.
[5] Barry and Dillon, *Proc. Roy. Irish Acad.*, 1943, **49**, *B*, 177.

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Estimation of the number of primary hydroxyl groups in oligo- and poly-saccharides has been accomplished by the well-established method of Oldham and Rutherford.[6] This method is based on the facts that the primary hydroxyl group in a sugar unit is esterified by toluene-*p*-sulphonyl chloride much faster than are the secondary hydroxyl groups, and that the primary tosyl groups can be replaced quantitatively by iodine under conditions which leave secondary tosyl groups unaffected. Subsequent determination of the iodine and the sulphur content of the product can be used to estimate the number of esterified primary and secondary hydroxyl groups respectively. Provided that esterification of the primary hydroxyl groups in a saccharide is complete, the method provides a means of estimating the number of free primary hydroxyl groups in the original saccharide. The method has found extensive application in the polysaccharide field, to cellulose and its derivatives,[7] starch,[8] and other polysaccharides.[9] Application of this method to yeast glucan should indicate the number of free hydroxyl groups and hence, by difference, the number of primary hydroxyl groups involved in 1 : 6-linkages.

The method was initially tested on amylose since this is known to contain no appreciable proportion of 1 : 6-linkages. Amylose from potato starch was treated with toluene-*p*-sulphonyl chloride in pyridine for various times, and the esterified amylose was isolated and treated with sodium iodide in hexane-2 : 5-dione at 115—120°. The product, after isolation, was analysed for iodine and sulphur. The results indicated that a temperature of 35° gave a reasonable rate of esterification and that the primary hydroxyl groups were completely esterified after 24 hr. (Table 1). (Incidentally, this

TABLE 1. *Esterification of amylose by toluene*-p-*sulphonyl chloride at* 35°.

Time of esterification (hr.)	Ester groups per anhydroglucose unit		Time of esterification (hr.)	Ester groups per anhydroglucose unit	
	Primary	Secondary		Primary	Secondary
6	0·66	0·21	30	0·99	1·04
12	0·80	0·50	35	1·01	1·09
21	0·98	0·84	50	0·99	1·19
24	1·01	0·94			

experiment provides additional evidence of the absence of 1 : 6-links from amylose.) The fact that the apparent degree of primary esterification did not increase after this time, whereas the degree of secondary esterification did increase, confirmed the view that the replacement of tosyl groups by iodine is limited to the primary positions under the conditions employed. The reliability of the method being established, two samples of yeast glucan

TABLE 2. *Esterification of yeast glucan by toluene*-p-*sulphonyl chloride.*

Time of esterification (hr.)	Ester groups per anhydroglucose unit		Time of esterification (hr.)	Ester groups per anhydroglucose unit	
	Primary	Secondary		Primary	Secondary
	At 65°, Specimen I			At 85°, Specimen I	
21	0·45	0·29	32	0·81	1·26
30	0·83	0·61	46	0·82	1·38
46	0·80	0·85	64	0·81	1·56
60	0·84	1·06			
72	0·84	1·14		At 80°, Specimen II	
84	0·82	1·18	24	0·82	1·07
			29	0·81	1·16

were examined by the same procedure. Esterification of yeast glucan proceeded more slowly than for amylose at 35° and the temperature was raised to 65° before a comparable rate was achieved (Table 2). Cellulose is also known to require a higher temperature in

[6] Oldham and Rutherford, *J. Amer. Chem. Soc.*, 1932, **54**, 366.
[7] Heuser, Heath, and Shockley, *J. Amer. Chem. Soc.*, 1950, **72**, 670 and references cited therein.
[8] Hess and Eveking, *Ber.*, 1934, **67**, 1908.
[9] Carson and Maclay, *J. Amer. Chem. Soc.*, 1948, **70**, 2220; Low and White, *ibid.*, 1943, **65**, 2430.

order to give a satisfactory rate of esterification; Honeyman [10] obtained complete esterification of primary hydroxyl groups in cellulose only after 16 hr. at 100°. At 65°, esterification of primary hydroxyl groups in yeast glucan reached a limiting value of 0·82 mol. per $C_6H_{10}O_5$ unit after 30 hr. and thereafter remained constant within the limits of experimental error, while esterification of secondary hydroxyl groups increased steadily. Raising the temperature to 85° did not increase this limit for specimen I, and the same result was observed with specimen II.

The margin of possible error in this method is dependent on a number of factors not all of which can be checked. For instance, the figures quoted are not corrected for the observation that the polyglucose content of the glucan was only 92·4%. The estimated content of 1 : 6-linkages could be 7—8% too high if all the non-hydrolysable material present in the original glucan persists in the acylated-iodinated product. No dubiety attaches however, to the conclusion that 10—20% of the glucosidic linkages in yeast glucan are 1 : 6-links, a conclusion which reinforces the earlier evidence.[1]

Experimental

Analytical Methods.—Iodine was determined by the bromine oxidation method.[11] For the determination of sulphur, the polysaccharide (100 mg.) was digested in a boiling-tube with perchloric acid (*d* 1·54; 4 ml.) under gentle reflux until frothing had ceased. Hydrogen peroxide (100-vol.; 0·1 ml.) was then added and the digestion continued, with addition of further portions of hydrogen peroxide, until the solution became colourless. After cooling, the contents of the tube were washed into a beaker, neutralised with 3N-sodium hydroxide, diluted to 100 ml., and made just acid with 3N-hydrochloric acid. The sulphate in this solution was estimated gravimetrically as barium sulphate by the usual procedure.

Polysaccharides.—Amylose was prepared from potato starch by the method of Hobson *et al.*[12] but, before use, was " activated " by precipitation from aqueous solution with pyridine, washing well with pyridine, and drying in a vacuum over phosphoric oxide. Specimen I of yeast glucan was that used by Peat *et al.*; [1] specimen II was prepared by the method of Bell and Northcote [4] but contained glycogen, as judged by iodine-staining. This specimen (25 g.) was therefore suspended in water (1 l.), and salivary amylase (50% saliva in water, centrifuged to remove mucins; 50 ml.) was added. Incubation at 35° for 24 hr. gave a product (23 g.), after filtration and washing, which was no longer stained by iodine. This gave glucose only on complete acid hydrolysis and had a polyglucose content of 92·4%.

Method.—The dried polysaccharide (0·5 g.) was suspended in dry pyridine (30 ml.) and toluene-*p*-sulphonyl chloride (6 g.) was added. The mixture was heated in a water bath and stirred under anhydrous conditions for the appropriate time (see Tables) and was then cooled to 0°. Excess of reagent was destroyed by adding a few ml. of water, the mixture was poured into iced water (500 ml.) and stirred for several hours, and the precipitated polysaccharide collected by filtration. The precipitate, after being washed with water, methanol, and ether and dried over phosphoric oxide, was heated at 115—120° for 7 hr. with an equal weight of anhydrous sodium iodide in dry hexane-2 : 5-dione (50 ml. per g.). The solvent was distilled off at 80—90° under reduced pressure and the residue was shaken with acetone (50 ml.) before being poured into iced water (1 l.). The precipitate was collected on a filter and washed with methanol, 0·1N-sodium thiosulphate, water, methanol, and finally with ether. After drying at 60° over phosphoric oxide, the product was analysed for sulphur and iodine. Extension of the time of heating with sodium iodide from 7 to 12 hr. indicated that iodination is complete in 7 hr.

We thank the Department of Scientific and Industrial Research for the award of a maintenance grant (to J. M. E.) and Dr. W. J. Whelan for helpful discussions.

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[10] Honeyman, *J.*, 1947, 168.
[11] E. P. Clark, " Semimicro Quantitative Organic Analysis," Academic Press Inc., New York, 1943, p. 62.
[12] Hobson, Pirt, Whelan, and Peat, *J.*, 1951, 801.

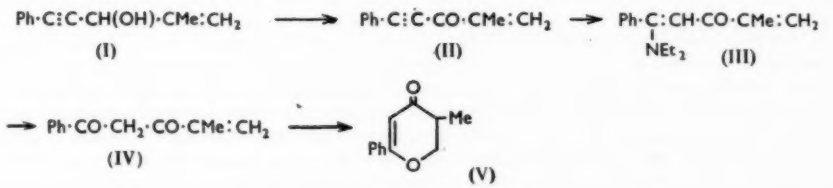
787. *The Structure and Synthesis of Bullatenone.*

By W. Parker, R. A. Raphael, and D. I. Wilkinson.

Bullatenone has been shown to be 2 : 3-dihydro-2 : 2-dimethyl-3-oxo-5-phenylfuran (X). This structure has been confirmed by synthesis from 2-methylbut-3-yn-2-ol.

In 1954 Brandt, Thomas, and Taylor[1] isolated an optically inactive crystalline unsaturated ketone (now named bullatenone) from the blistered-leaf myrtle (*Myrtus bullata*), a shrub endemic to New Zealand. Degradative studies led them to propose the plausible dihydro-γ-pyrone formulation (V) for the compound; the alternative with the methyl group at position 2 was thought less likely but was not conclusively excluded. The main objection to this constitution is the stability of bullatenone to selenium dioxide, a reagent which should readily convert such a compound into the corresponding γ-pyrone.

Both of these dihydro-γ-pyrones have now been synthesised in the following manner. Interaction of 2-methylacraldehyde and phenylethynylmagnesium bromide gave the alcohol (I) which was oxidised to the corresponding ketone (II) with chromium trioxide. Indirect hydration of the triple bond of ketone (II) was achieved by addition of diethylamine and acid hydrolysis of the intermediate enamine (III) to the β-diketone (IV). Initial



nucleophilic addition to the triple bond rather than to the similarly activated double bond is predictable from previous work.[2] Cyclisation of the β-diketone (IV) by concentrated sulphuric acid gave the dihydropyrone (V). The corresponding 2-methyl-substituted analogue was obtained in similar fashion by employing crotonaldehyde in the initial condensation. As expected, both of these dihydropyrones were smoothly dehydrogenated to the respective γ-pyrones by selenium dioxide. Neither of the dihydropyrones was identical with bullatenone.

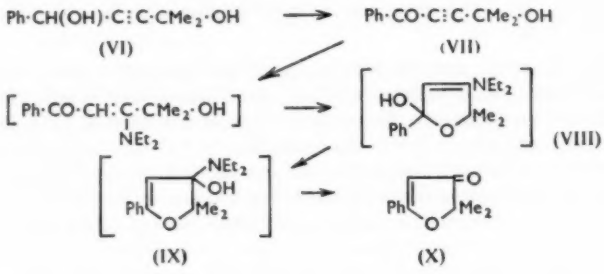
Owing to the great courtesy of Dr. W. I. Taylor, who not only handed over the problem but also kindly provided us with a generous specimen, we were enabled to re-examine the structure of bullatenone. In carbon tetrachloride the carbonyl stretching frequency appeared at 1705 cm.$^{-1}$ (suggestive of an αβ-unsaturated ketone in a five-membered ring) rather than at the previously reported[1] value of 1681 cm.$^{-1}$ (solid film). The infrared spectrum (KCl pellet) showed further diagnostic absorption at 1604 cm.$^{-1}$ (five-membered cyclic enol ether), 1360 and 1378 cm.$^{-1}$ (CMe_2), and a series of sharp bands appeared between 800 and 1700 cm.$^{-1}$ strongly indicative of the presence of a 2 : 3-dihydro-3-oxofuran system.[3] These results suggested the isomeric structure 2 : 3-dihydro-2 : 2-dimethyl-3-oxo-5-phenylfuran (X) for bullatenone. This formulation explains the resistance of bullatenone to oxidation by selenium dioxide and the lack of optical activity.

This structure was confirmed by synthesis. Reaction of benzaldehyde with the Grignard derivative of 2-methylbut-3-yn-2-ol produced the acetylenic diol (VI), which, by oxidation of the secondary hydroxyl group, furnished the hydroxy-ketone (VII). Addition of diethylamine to the latter, followed by distillation, unexpectedly gave the crystalline

[1] Brandt, Thomas, and Taylor, *J.*, 1954, 3425.
[2] Bowden, Braude, Jones, and Weedon, *J.*, 1946, 45.
[3] Eugster, *Helv. Chim. Acta*, 1957, **40**, 2462.

XUM

dihydrofuran (X) directly. A rationalisation of this result can be visualised by an oxotropic rearrangement of the cyclic tautomer (VIII) of the diethylamine adduct followed by the expected ready extrusion of diethylamine from the product (IX). The dihydrooxofuran (X) thus obtained proved identical with bullatenone. The occurrence of this



system in a natural product does not seem to have been encountered before and the biogenesis of bullatenone is not easy to reconcile with either the acetate or the mevalonate hypothesis.

Experimental

2-Methyl-5-phenylpent-1-en-4-yn-3-ol (I).—Phenylacetylene (30·6 g.) in dry ether (50 ml.) was added to a stirred solution of ethylmagnesium bromide (from magnesium, 7·92 g.) in ether (250 ml.), and the whole heated under reflux, with stirring, for 2 hr. The solution was cooled to −10° and an excess of redistilled 2-methylacraldehyde (24 g.) in ether (75 ml.) was added during 20 min. The mixture was stirred for 2 hr. at room temperature and finally heated to reflux. The cooled mixture was decomposed with 10% v/v aqueous acetic acid (120 ml.), and the ethereal phase was washed with saturated sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Evaporation of the solvent and fractionation of the crude product through a short Vigreux column gave a fore-run of phenylacetylene, b. p. 35—40°/0·07 mm., and then *2-methyl-5-phenylpent-1-en-4-yn-3-ol* as a colourless oil rapidly becoming yellow (35·5 g., 69%), b. p. 104—114°/0·07 mm. The analytical sample had b. p. 100—102°/0·15 mm., n_D^{25} 1·5666, $\lambda_{max.}$ (in chloroform) 250 mμ (ε 14,600) (Found: C, 83·9; H, 7·0. $C_{13}H_{13}O$ requires C, 83·7; H, 7·0%).

2-Methyl-5-phenylpent-1-en-4-yn-3-one (II).—A stirred solution of the above alcohol (26·3 g.) in acetone (50 ml.) was treated at 0—10° with chromic acid [from chromium trioxide (10·5 g.), water (30 ml.), and concentrated sulphuric acid (8·5 ml.)] during 15 min. Then stirring was continued for another hour at room temperature, and water and ether were next added. The aqueous layer was washed with ether (2 × 100 ml.), and the combined ethereal extracts were washed with dilute sodium hydrogen carbonate solution and dried ($MgSO_4$). Removal of the ether gave the *ketone* as a solid which was purified first by distillation, b. p. 86—110°/0·1 mm. (16·6 g., 63%), and then by crystallisation from aqueous methanol whence it formed prisms, m. p. 54·5—55·5°, $\lambda_{max.}$ (in ethanol) 298 mμ (ε 12,400) (Found: C, 84·8; H, 6·05. $C_{12}H_{10}O$ requires C, 84·7; H, 5·9%).

The 2 : 4-*dinitrophenylhydrazone*, m. p. 200·5—202°, crystallised from chloroform–ethyl acetate in orange platelets, $\lambda_{max.}$ (in chloroform) 268, 300, 384 mμ (ε = 20,200, 9000, and 30,900 respectively) (Found: C, 61·1; H, 3·9; N, 15·2. $C_{18}H_{14}O_4N_4$ requires C, 61·7; H, 4·05; N, 16·0%).

1-Diethylamino-4-methyl-1-phenylpenta-1 : 4-dien-3-one (III).—Diethylamine (1·5 g.) in ethanol (10 ml.) was added slowly to a stirred solution of the above ketone (3·4 g.) in ethanol (15 ml.) at 0°. The stirring was continued at room temperature for 1 hr. Removal of the ethanol and distillation of the residual syrup furnished the yellow *enamine* (2·12 g., 44%), b. p. 132—136°/0·15 mm., n_D^{25} 1·5830, $\lambda_{max.}$ (in chloroform) 332 mμ (ε 11,900) (Found: C, 79·1; H, 8·45; N, 5·9. $C_{16}H_{21}ON$ requires C, 78·9; H, 8·7; N, 5·75%).

4-Methyl-1-phenylpent-4-ene-1 : 3-dione (IV).—The enamine (2·12 g.) was shaken with 2N-sulphuric acid (30 ml.) for 6 hr. and the organic material then isolated by ether. The required

dione was obtained by distillation as a light yellow oil (0·77 g., 47%), b. p. 98—101°/0·1 mm., n_D^{25} 1·6129, $\lambda_{max.}$ (in *n*-hexane) 225, 245 (inflexion) and 320 mμ (ε 7500, 6800, and 13,300 respectively) (Found: C, 76·6; H, 6·45. $C_{12}H_{12}O_2$ requires C, 76·55; H, 6·45%).

This compound gave a strong colour with aqueous ferric chloride and also formed a copper salt which crystallised from aqueous ethanol in green cubic crystals, m. p. 164°.

2 : 3-*Dihydro*-3-*methyl*-6-*phenyl*-4-*pyrone* (V).—A solution of the above diketone (230 mg.) in concentrated sulphuric acid (3 ml.) was held at room temperature for 24 hr. It was then poured into ice-cold water and extracted with ether, and the ethereal extract washed with saturated sodium hydrogen carbonate solution, then water, and dried ($MgSO_4$). After removal of the solvent the residual red solid was chromatographed in benzene on a short column of alumina (grade III). Elution with chloroform–benzene (1 : 9) and recrystallisation of the isolated product from light petroleum (b. p. 60—80°) afforded the *dihydropyrone* as needles, m. p. 96—97° (100 mg., 43%), $\lambda_{max.}$ (in ethanol) 222, 242, and 296 (ε 8400, 5500, and 17,000 respectively) (Found: C, 76·6; H, 6·1. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%).

The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in red needles m. p. 210—212°, $\lambda_{max.}$ (in ethanol) 396 mμ (ε 32,500) (Found: C, 58·95; H, 4·55; N, 15·2. $C_{18}H_{16}O_5N_4$ requires C, 58·7; H, 4·4; N, 15·2%).

5-*Methyl*-2-*phenyl*-4-*pyrone*.—The above dihydropyrone (75·2 mg.) and selenium dioxide (44·4 mg.) were heated under reflux in glacial acetic acid (10 ml.) for 2 hr. The cooled solution was filtered through a pad of " Celite " and evaporated to dryness. The solid residue was dissolved in benzene and adsorbed on a short column of alumina (grade III). Elution with chloroform–benzene (1 : 3) followed by crystallisation of the isolated material from light petroleum (b. p. 60—80°) gave 5-*methyl*-2-*phenyl*-4-*pyrone* in long needles, m. p. 132—133° (42 mg., 56%), $\lambda_{max.}$ (in ethanol) 273 mμ (ε 19,800) (Found: C, 77·4; H, 5·6. $C_{12}H_{10}O_2$ requires C, 77·40; H, 5·4%).

1-*Phenylhex*-4-*en*-1-*yn*-3-*ol*.—Phenylacetylene (30·6 g.) in dry ether (50 ml.) was added to a chilled solution of ethylmagnesium bromide (prepared from magnesium, 7·92 g.), and the solution heated under reflux for 3 hr. Excess of freshly distilled crotonaldehyde (24 g.) in ether (75 ml.) was then added at 0° and the stirring continued for 2 hr. The mixture was worked up as in the above cognate preparation to give the pale yellow *alcohol* (31 g., 60%), b. p 140—146°/0·15 mm., n_D^{22} 1·5850 (Found: C, 83·5; H, 6·85. $C_{12}H_{12}O$ requires C, 83·7; H, 7·0%), $\lambda_{max.}$ (in ethanol) 242 mμ (ε 20,000).

1-*Phenylhex*-4-*en*-1-*yn*-3-*one*.—A stirred solution of the alcohol (26·3 g.) in acetone (50 ml.) was chilled to −10° and treated dropwise with chromic acid [from chromium trioxide (10·5 g.), water (30 ml.), and concentrated sulphuric acid (8·5 ml.)]. The mixture was warmed to room temperature and stirred for 1 hr. Isolation by ether and distillation gave the required *ketone* (16 g., 61%), b. p. 120—124°/1 mm., $n_D^{22.5}$ 1·5938, $\lambda_{max.}$ (in ethanol) 292 mμ (ε 12,200). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in orange-red needles, m. p. 197—198° (Found: C, 61·65; H, 4·05; N, 16·1. $C_{18}H_{14}O_4N_4$ requires C, 61·7; H, 4·05; N, 16·0%).

1-*Phenylhex*-4-*ene*-1 : 3-*dione*.—A solution of diethylamine (1·5 g.) in ethanol (10 ml.) was added dropwise with stirring to the ketone (3·4 g.) in ethanol (15 ml.) at 0°. After 1 hr. at room temperature the solvent was removed and the residue distilled, to furnish the orange diethylamine adduct (3·2 g., 66%), b. p. 136°/0·25 mm., n_D^{24} 1·6031. This adduct (3·4 g.) in acetone (15 ml.) was shaken with 3N-sulphuric acid (30 ml.) for 9 hr., then diluted with water. Isolation with ether gave a yellow semi-solid product (3·15 g.) from which one *isomer* of the dione was isolated by crystallisation from light petroleum (b. p. 30—60°) as needles, m. p. 58—59° (1·7 g.) (Found: C, 76·55; H, 6·5. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·45%), $\lambda_{max.}$ (in ethanol) 228, 248 (inflexion), 340 mμ (ε 8800, 7400, and 21,800 respectively). This isomer gave a strong red colour with ferric chloride solution, and a copper salt crystallising in plates, m. p. 239—242°, from chloroform–ether. From the mother-liquors a liquid *isomer* (1·4 g.) of the dione was isolated by distillation, having b. p. 102—104°/0·15 mm., n_D^{23} 1·6220 (Found: C, 76·9; H, 6·6%). This isomer gave a strong red colour with ferric chloride, but no copper salt could be prepared.

2 : 3-*Dihydro*-2-*methyl*-6-*phenyl*-4-*pyrone*.—A solution of the above diketone (m. p. 58°) (500 mg.) in concentrated sulphuric acid (6 ml.) was kept at room temperature for 24 hr., then poured on ice and worked up as in the above cognate experiment. The dihydropyrone (263 mg., 53%) crystallised from light petroleum (b. p. 60—80°) in plates, m. p. 62—63° (Found: C, 76·6; H, 6·5. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·45%), $\lambda_{max.}$ (in ethanol) 222, 242, 298 mμ

(ε 6100, 8000, and 16,900 respectively). Cyclisation of the liquid dione with concentrated sulphuric acid gave the same dihydropyrone, m. p. and mixed m. p. 62°, but in much lower yield.

5-Bromo-2 : 3-dihydro-2-methyl-6-phenyl-4-pyrone.—The above dihydropyrone (78 mg.) in carbon tetrachloride (10 ml.) was treated with bromine (64 mg.) in carbon tetrachloride for 15 min. at room temperature. After removal of the solvent the mixture was refluxed with collidine (5 ml.) for 15 min., poured into water and extracted with ether, and the ethereal extract was dried ($MgSO_4$). Removal of the solvent gave a brown oil which was chromatographed on a short column of alumina (grade III). Elution with benzene furnished the *bromo-derivative* (36 mg., 35%) which recrystallised in needles, m. p. 106—107° [from light petroleum (b. p. 60—80°)] (Found: C, 54·1; H, 3·95. $C_{12}H_{11}O_2Br$ requires C, 53·8; H, 4·1%), $\lambda_{max.}$ (in ethanol) 306 mμ (ε 11,500).

2-Methyl-6-phenyl-4-pyrone.—2 : 3-Dihydro-2-methyl-6-phenyl-4-pyrone (94 mg.) was refluxed in glacial acetic acid (15 ml.) with selenium dioxide (55·5 mg.) for 2 hr. The cooled mixture was filtered through " Celite," then evaporated to dryness and the residual red solid was chromatographed in benzene on alumina (grade III). Elution with benzene removed traces of selenium; changing the eluant to benzene–chloroform (1 : 1) gave a viscous brown oil (58 mg.) which was sublimed at 110°/0·1 mm. The resulting yellow solid crystallised from light petroleum (b. p. 60—80°) to furnish 2-methyl-6-phenyl-4-pyrone in needles, m. p. 85—86° (lit.,[4] m. p. 83—84°).

4-Methyl-1-phenylpent-2-yne-1 : 4-diol (VI).—2-Methylbut-3-yn-2-ol (42 g.) in an equal volume of anhydrous ether was added dropwise to a stirred solution of ethylmagnesium bromide (from magnesium, 24 g.) in dry ether (400 ml.) held at 0°. After 30 minutes' heating under reflux the solution was cooled and treated with benzaldehyde (53 g.) in an equal volume of dry ether, and the mixture refluxed for a further 2 hr. The solid complex which had been precipitated was decomposed with a saturated ammonium chloride solution, the organic layer separated, washed with water, and dried ($MgSO_4$), and the solvent removed to furnish the *diol* as a crystalline mass (74·8 g., 79%). The diol crystallised in needles, m. p. 75—76°, from benzene–light petroleum (b. p. 60—80°) (Found: C, 76·0; H, 7·45. $C_{12}H_{14}O_2$ requires C, 75·75; H, 7·4%).

4-Hydroxy-4-methyl-1-phenylpent-2-yn-1-one (VII).—A stirred solution of 4-methyl-1-phenylpent-2-yne-1 : 4-diol (19 g.) in acetone (35 ml.) was treated dropwise with a chromic acid solution [from chromium trioxide (7·3 g.), water (20 ml.), and concentrated sulphuric acid (6 ml.)], the temperature of the mixture being held at 0—5°. After one hour's further stirring at room temperature the mixture was diluted with water and extracted with ether (3 × 75 ml.) and the ethereal extract washed with sodium hydrogen carbonate solution and water and dried ($MgSO_4$). Evaporation and distillation furnished the *keto-alcohol* as a pale yellow oil, b. p. 138—139°/0·4 mm., n_D^{22} 1·5529, $\lambda_{max.}$ (in ethanol) 264 mμ (ε 14,700). Treatment with hydrazine sulphate and sodium carbonate by Bowden and Jones's procedure [5] gave the corresponding *pyrazole* which crystallised in needles, m. p. 153—154·5°, from ethyl acetate (Found: C, 71·55; H, 6·75; N, 13·8. $C_{12}H_{14}ON_2$ requires C, 71·3; H, 7·0; N, 13·8%).

2 : 3-Dihydro-2 : 2-dimethyl-3-oxo-5-phenylfuran (X).—A stirred solution of the preceding hydroxy-ketone (3·76 g.) in ethanol (20 ml.) was treated dropwise with an ethanolic solution of diethylamine (1·46 g.) and stirring continued for 30 min. Removal of solvent under reduced pressure and distillation gave a yellow oil, b. p. 110°/0·1 mm., which solidified. Crystallisation from light petroleum (b. p. 60—80°) furnished *2 : 3-dihydro-2 : 2-dimethyl-3-oxo-5-phenylfuran* (1·11 g., 30%) in needles, m. p. 67·5—68·5° undepressed on admixture with bullatenone (Found: C, 76·8; H, 6·7. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%), $\lambda_{max.}$ (in ethanol) 242, 296, 304 mμ (ε 8000, 16,000, and 16,000 respectively). The infrared spectra of substance (X) and bullatenone were superimposable. Modification of the procedure by substituting treatment with dilute sulphuric acid at room temperature for the distillation gave a higher yield (2 g.). The 2 : 4-dinitrophenylhydrazone prepared in the usual manner crystallised from ethanol in dark red needles, m. p. 243—246°, $\lambda_{max.}$ (in ethanol) 412 mμ (ε 26,800); the m. p. was undepressed on admixture with bullatenone 2 : 4-dinitrophenylhydrazone. Treatment of the ketone with bromine in carbon tetrachloride gave the 4-bromo-derivative which was crystallised from light petroleum (b. p. 40—60°) and sublimed at 75°/10^{-4} mm., to yield needles, m. p. 79·5—80·5° (lit.,[1] m. p. 74°)

[4] Franzosini, Traverso, and Sanesi, *Ann. Chim.* (*Italy*), 1953, **45**, 128.
[5] Bowden and Jones, *J.*, 1946, 953.

(Found: C, 54·15; H, 4·3; Br, 29·9. Calc. for $C_{12}H_{11}O_2Br$: C, 53·95; H, 4·15; Br, 29·75%), $\lambda_{max.}$ (in ethanol) 224, 246, and 314 mμ (ε 6800, 9600, and 16,500 respectively).

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788. *The Effect of the Nitro-group on the Reactivity of the Diphenyl Nucleus in Nitration. Competitive Nitration of Nitrodiphenyls and Benzene by Nitric Acid in Acetic Anhydride.*

By Y. MIZUNO and O. SIMAMURA.

Competitive nitration of nitrodiphenyls and benzene has been carried out by nitric acid in acetic anhydride at 0°. The proportions of isomeric dinitrodiphenyls produced and the partial rate factors show that the polar effect of the nitrophenyl groups is similar to that of halogen atoms with mesomeric electron-releasing and inductive electron-attracting effect. The theoretical implication of the change in the *ortho* : *para* ratio of the nitration products of isomeric nitrodiphenyls is discussed.

NITRODIPHENYLS undergo electrophilic substitution, such as nitration,[1,2] bromination,[1,3] and acetylation,[4] at the 2- and 4-position of the unsubstituted ring. These facts led many workers [5] to adopt the view that the two nuclei of diphenyl act independently in substitution. Later, evidence from physical measurements including dipole moments,[6] *X*-ray crystal analysis,[7] and absorption spectra [8] showed, however, that the lack of conjugation between the two nuclei in the diphenyl system was not complete. That the effect of substituents is also transmitted through the diphenyl system in chemical reactions was shown by more recent studies of the dissociation constants of 4'-substituted diphenyl-4-carboxylic acids [9] and 4-hydroxy-4'-nitrodiphenyl [10] and of the rates of nucleophilic substitution of 4-bromo-3 : 4'-dinitrodiphenyl by piperidine [11] and of alkaline hydrolysis of substituted ethyl diphenyl-4-carboxylates.[12] In electrophilic substitution, 2- and 4-nitrodiphenyls are chlorinated in aqueous acetic acid at a rate some two-thousand times slower than diphenyl,[13] showing that the deactivating influence of the nitro-group is relayed to the unsubstituted nucleus. To provide further evidence of a quantitative nature, we now report the competitive nitration of each of three isomeric nitrodiphenyls and benzene.

The nitrations were carried out with nitric acid in acetic anhydride at 0°. The experimental conditions and results are summarized in Tables 1, 2, and 3. From the amounts of dinitrodiphenyls and nitrobenzene produced the relative rates of the nitration of nitrodiphenyls with respect to benzene were calculated, according to the method of Ingold and

[1] Blakey and Scarborough, *J.*, 1927, 3000.
[2] Gull and Turner, *J.*, 1929, 491; Maki and Ohayashi, *J. Chem. Soc. Japan, Chem. Ind. Sect.*, 1951, **54**, 375.
[3] Le Fèvre and Turner, *J.*, 1926, 2041; Case, *J. Amer. Chem. Soc.*, 1938, **60**, 424.
[4] Grieve and Hey, *J.*, 1933, 968.
[5] Le Fèvre and Turner, *J.*, 1928, 245; Burkhardt, Horrex, and Jenkins, *J.*, 1936, 1654; Campbell, Anderson, and Gilmore, *J.*, 1940, 446.
[6] Le Fèvre and Le Fèvre, *J.*, 1936, 1130.
[7] Dhar, *Indian J. Physics*, 1932, **7**, 43.
[8] Pickett, Walter, and France, *J. Amer. Chem. Soc.*, 1936, **58**, 2296; Gillam and Hey, *J.*, 1939, 1170; Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 1658; Williamson and Rodebush, *ibid.*, p. 3018.
[9] Berliner and Blommers, *ibid.*, 1951, **73**, 2479.
[10] Kreiter, Bonner, and Eastman, *ibid.*, 1954, **76**, 5770.
[11] Berliner, Newman, and Riaboff, *ibid.*, 1955, **77**, 478.
[12] Berliner and Liu, *ibid.*, 1953, **75**, 2417.
[13] Hartman and Robertson, *J.*, 1945, 891.

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TABLE 1. *Competitive nitration of* 4*-nitrodiphenyl and benzene at* 0°. (*The amounts of compounds taken or formed are expressed in millimoles.*)

Experiment no.:	1	2	3	
Benzene taken	100	25·0	25·0	
4-Nitrodiphenyl taken	25·0	25·0	25·0	
Nitric acid	100	120	120	
Acetic anhydride	1400	1500	1500	
Reaction time (hr.)	72	42	45	
Nitrobenzene formed	20·1	12·2	13·9	
Dinitrodiphenyls formed	1·76	4·95	5·56	
Isomer composition (%)				Mean
2 : 4′-	—	35	34	34·5
3 : 4′-	—	0·5	0	0·3
4 : 4′-	—	64	66	65
Relative rate	0·33	0·33	0·32	0·33

TABLE 2. *Competitive nitration of* 3*-nitrodiphenyl and benzene at* 0°. (*The amounts of compounds taken or formed are expressed in millimoles.*)

Experiment no.:	4	5	6	
Benzene taken	25·0	25·0	0	
3-Nitrodiphenyl taken	25·0	25·0	12·9	
Nitric acid	37·5	25	20	
Acetic anhydride	800	500	250	
Reaction time (hr.)	26	7	7	
Nitrobenzene formed	4·11	5·20	0	
Dinitrodiphenyls formed	3·99	5·64	5·60	
Isomer composition (%)				Mean
2 : 3′-	—	46	44	45
3 : 4′-	—	54	56	55
Relative rate	0·97	1·09	—	1·03

TABLE 3. *Competitive nitration of* 2*-nitrodiphenyl and benzene at* 0°. (*The amounts of compounds taken or formed are expressed in millimoles.*)

Experiment no.:	7	8	9	
Benzene taken	25·0	25·0	25·0	
2-Nitrodiphenyl taken	25·0	25·0	25·0	
Nitric acid	20	23	23	
Acetic anhydride	400	400	400	
Reaction time (hr.)	24	18	18	
Nitrobenzene formed	5·28	6·05	5·12	
Dinitrodiphenyl formed	1·79	2·04	1·79	
Isomer composition (%)				Mean
2 : 2′-	31	29	30	30
2 : 3′-	2	4	4	3
2 : 4′-	67	67	66	67
Relative rate	0·31	0·31	0·32	0·31

TABLE 4. *Partial rate factors for the nitration of nitrodiphenyls and* ortho : para- *ratios of the products.*

	Partial rate factors			
Nuclear position:	2′	3′	4′	*o* : *p*
4-Nitrodiphenyl	0·35	<0·01	1·3	0·54
3-Nitrodiphenyl	1·4	0	3·4	0·82
2-Nitrodiphenyl	0·28	0·03	1·2	0·46
Diphenyl [15]	41	<0·6	38	2·2

Shaw.[14] The relative rates and the proportions of isomeric dinitrodiphenyls formed gave the partial rate factors for nitration of nitrodiphenyls, the rate constants of separate nuclear positions of nitrodiphenyls relative to one nuclear position of benzene being taken

[14] Ingold and Shaw, *J.*, 1927, 2918.

as unity. The values are shown in Table 4, in which those for nitration of diphenyl[15] itself are included for comparison.

The present results show that, although the substitution takes place at positions 2 and 4 of the nucleus from which the nitro-group is absent, nitrodiphenyls are largely deactivated in comparison with diphenyl, though only slightly deactivated with respect to benzene. This situation is very similar to those observed in the nitrations of compounds with substituents which are classed as type 3 $(-I + T)$ by Ingold and Shaw,[16] such as halogenobenzenes, cinnamic acid,[17] benzyl chloride, and ethyl phenylacetate, and the present case offers a further example. The *ortho-para*-orientation is attributed to the electromeric electron-release due to the polarisable π-electrons in the nitrophenyl group. An explanation for this orientation in terms of resonance structures contributing to the transition state has been given by Berliner and Blommers.[9] The deactivation with respect to diphenyl and even to benzene is obviously caused by relay of the electron-attracting effect of the nitro-group through the 1 : 1′-linkage. The orientation in nitrobenzene shows that the deactivating electron-attraction is less from a 3-nitro- than from a 2- or 4-nitro-group, resulting in 3-nitrodiphenyl's being appreciably more reactive than the 2- or the 4-isomer.

The *ortho* : *para* ratio in which the diphenyls are nitrated falls in the order diphenyl > 3- > 4- > 2-nitrodiphenyl, as shown in Table 4. According to the generally accepted view[18] that the *ortho* : *para* ratio decreases with the increasing electron-attracting inductive effect of the orienting substituent, the above order suggests that this effect increases in the order phenyl < 3- < 4- < 2-nitrophenyl. This order is in conformity with the nature of transmission of the polar effects of these groups, except for the 2-nitrophenyl group (upon which result some doubt could be thrown). Ingold[18] has attributed the activation of the *ortho*- with respect to the *para*-position of nitrobenzene towards the electrophilic reagent to the selective deactivation of the latter compared with the former position. If this view is accepted, the 2-nitrophenyl group is to be considered less electron-attracting than the 4-nitrophenyl group. Thus the *ortho* : *para* ratio for 2-nitrodiphenyl would be expected to be larger than that for the 4-nitro-isomer, *viz.*, 0·54. Actually it was found to be 0·46. The discrepancy is probably due to operation on the 2′-position in 2-nitrodiphenyl of steric hindrance due to the presence of the 2-nitro-group.

Experimental

Reagents.—4-Nitrodiphenyl was prepared by nitration of diphenyl with nitric acid in acetic acid as described by Bell, Kenyon, and Robinson.[19] Recrystallization from ethanol gave pure 4-nitrodiphenyl, m. p. 113·5°. 3-Nitrodiphenyl, m. p. 61° (from methanol), was synthesized according to the method of France, Heilbron, and Hey [20] by decomposing *m*-nitro-*N*-nitroso-acetanilide in benzene. 2-Nitrodiphenyl, m. p. 37° (from methanol), was obtained by Elks, Haworth, and Hey's method,[21] the action of sodium acetate on a stirred mixture of diazotized *o*-nitroaniline and benzene. Benzene was purified by shaking with concentrated sulphuric acid, fractionally distilling it through a Vigreux column, and finally freezing it. Nitric acid was prepared by distilling commercial fuming nitric acid from concentrated sulphuric acid at ordinary pressure, and then twice at 20 mm. The faintly yellow distillate was stored in a refrigerator. Acetic anhydride was purified by fractional distillation (b. p. 140°).

Competitive Nitration of 4-Nitrodiphenyl and Benzene.—A typical experiment (No. 2 in Table 1) was carried out as follows: Nitric acid (5 ml.) in acetic anhydride (10 ml.) was added dropwise at 0° to a stirred solution of 4-nitrodiphenyl (4·981 g.) and benzene (1·985 g.) in acetic anhydride (140 ml.). The reaction was allowed to proceed for 42 hr. at 0°. The mixture was

[15] Simamura and Mizuno, *Bull. Chem. Soc. Japan*, 1957, **30**, 196.
[16] Ingold and Shaw, *J.*, 1949, 575.
[17] Bordwell and Rohde, *J. Amer. Chem. Soc.*, 1948, **70**, 1191.
[18] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N.Y., 1953, p. 261.
[19] Bell, Kenyon, and Robinson, *J.*, 1926, 1239.
[20] France, Heilbron, and Hey, *J.*, 1939, 1288.
[21] Elks, Haworth, and Hey, *J.*, 1940, 1284.

then poured into ice-water (400 ml.) and left overnight. The crystalline precipitate was filtered off, dried, and weighed (5·145 g.). About one-third (1·681 g.) of this solid was chromatographed in 100 ml. of 1 : 1 light petroleum–benzene on alumina (2·5 × 30 cm.). Elution with the same solvent gave unchanged 4-nitrodiphenyl and then 2 : 4′-dinitrodiphenyl (0·124 g.), m. p. and mixed m. p. 92—93°. Subsequent elution with benzene afforded 4 : 4′-dinitrodiphenyl (0·252 g.), m. p. and mixed m. p. 232—233°. The filtrate from the crystalline precipitate was neutralized with sodium hydrogen carbonate, and extracted with ether (800 ml.). The ethereal extract was washed with dilute sodium hydroxide solution and then with water and dried ($CaCl_2$), and the ether was distilled off through a Vigreux column. When concentrated to about 50 ml., the solution was shaken with an aqueous solution (25 ml.) of sodium sulphite (3 g.) and sodium hydrogen carbonate (0·7 g.) in order to remove tetranitromethane.[22] The ethereal solution was further concentrated to about 5 ml. The residue was dissolved in ethanol, and the solution made up to 25 ml. and analyzed for nitro-groups by titrating aliquot parts (1·00 ml.) with standard titanium trichloride and ferric alum solution.[23] The remainder of the ethanolic solution was distilled at 20 mm., with occasional additions, into the distilling flask, of a little aniline as carrier for nitrobenzene, until nitrobenzene was completely removed, giving an oily mixture of aniline, 4-nitrodiphenyl, and dinitrodiphenyls. The mixture was dissolved in ether and the solution was extracted with dilute hydrochloric acid. The ether was removed, the residue dissolved in ethanol, and the solution made up to 25 ml. and analyzed for nitro-groups on aliquot portions (1·00 ml.). The difference between the two values for the nitro-group determination, before and after the removal of nitrobenzene, represents the amount of the nitrobenzene formed. The remaining solution was evaporated and the residue comprising eight-tenth parts of the dinitrodiphenyls contained in the original filtrate was chromatographed in light petroleum–benzene on alumina. Elution with the same solvent mixture gave 4-nitrodiphenyl, 2 : 4′- (41 mg.), 3 : 4′- (4 mg.), and 4 : 4′-dinitrodiphenyl (7 mg.) in succession. The 3 : 4′-dinitrodiphenyl was identified by means of its m. p. and ultraviolet absorption spectrum in ethanolic solution (cf. Table 5). Thus the total amount of dinitrodiphenyls produced was found to be 1·210 g., consisting of 64% of 4 : 4′-, 35% of 2 : 4′-, and 0·5% of 3 : 4′-isomer. The above procedure for estimating the various products was checked by using an artificial mixture of known quantities of these compounds, with the following results:

	Taken	Found		Taken	Found
Acetic anhydride	150 ml.	—	2 : 4′-Dinitrodiphenyl	0·361 g.	0·352 g.
Benzene	0·805 g.	—	3 : 4′-Dinitrodiphenyl	0·011 g.	0·010 g.
4-Nitrodiphenyl	3·752 g.	3·747 g.	4 : 4′-Dinitrodiphenyl	0·683 g.	0·680 g.
Nitrobenzene	1·225 g.	1·211 g.			

Competitive Nitration of 3-*Nitrodiphenyl and Benzene.*—The nitration and the determination of the products were carried out as described above for the competitive nitration of 4-nitrodiphenyl and benzene. Chromatography yielded 2 : 3′-dinitrodiphenyl, m. p. 120°, and 3 : 4′-dinitrodiphenyl, m. p. 187—189°, both undepressed on admixture with authentic specimens. 3 : 3′-Dinitrodiphenyl could not be detected.

TABLE 5. *Absorption spectra* ($10^{-3}\varepsilon$) *of* 4 : x′-*dinitrodiphenyls in* 96% *ethanol.*

λ (mμ)	$x' = 2'$	$x' = 3'$	$x' = 4'$	λ (mμ)	$x' = 2'$	$x' = 3'$	$x' = 4'$	λ (mμ)	$x' = 2'$	$x' = 3'$	$x' = 4'$
220	17·39	19·25	11·30	270	14·35	17·55	9·90	308	7·47	14·45	25·90
230	9·89	15·00	6·75	285	12·67	19·50	19·00	315	5·68	11·03	25·20
245	9·03	9·14	3·82	300	9·57	17·58	25·20	330	2·52	4·69	15·82
260	12·89	13·60	5·29								

Competitive Nitration of 2-*Nitrodiphenyl and Benzene.*—A mixture of 2-nitrodiphenyl and benzene was nitrated under the conditions shown in Table 3. The mixture was added to ice-water (400 ml.) and left overnight. The oily precipitate was extracted with ether after the mixture had been neutralized with sodium hydrogen carbonate. The ethereal extract was concentrated and any tetranitromethane removed. Nitrobenzene was distilled from the mixture as described above and estimated titanometrically. Chromatography of the remaining mixture gave a mixture of dinitrodiphenyls, which was weighed and analyzed for nitrogen (correct value for $C_{12}H_8O_4N_2$). The isomer composition in which the three dinitrodiphenyls

[22] Ingold and Smith, *J.*, 1938, 905.
[23] Cumming, Hopper, and Wheeler, "Systematic Organic Chemistry," Constable & Co., Ltd., London, 4th edn., 1950, p. 494.

were produced was estimated spectrophotometrically, absorptions in ethanolic solution at 225, 227·5, 280, and 285 mμ being used (cf. Table 6). Lambert–Beer's law was obeyed and tests with artificial mixtures of known compositions showed that this analytical procedure was satisfactory; analysis of a mixture of, *e.g.*, 2 : 2′- (26·5%), 2 : 3′- (5·0%), and 2 : 4′-dinitrodiphenyl (68·5%) gave values of 26·8%, 6·1%, and 67·1% respectively.

TABLE 6. *Absorption spectra* ($10^{-3}\varepsilon$) *of* 2 : x′-*dinitrodiphenyls in* 96% *ethanol.*

λ (mμ)	x′ = 2′	x′ = 3′	x′ = 4′	λ (mμ)	x′ = 2′	x′ = 3′	x′ = 4′	λ (mμ)	x′ = 2′	x′ = 3′	x′ = 4′
222·5	18·60	23·50	15·48	255	11·25	12·50	11·80	290	4·63	4·49	11·60
225	16·48	23·40	13·57	260	11·50	12·45	12·89	295	4·05	3·92	10·62
227·5	14·28	22·95	11·28	270	9·85	10·03	14·35	300	3·56	3·48	9·57
235	10·03	19·79	8·14	280	6·84	6·79	13·58	310	2·72	2·56	7·13
245	9·77	12·88	9·03	285	5·50	5·35	12·67				

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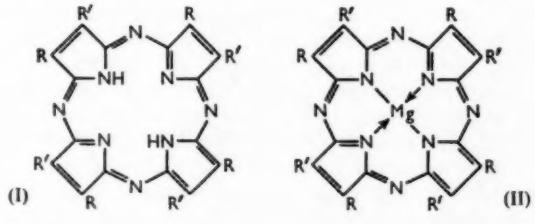
789. *Conjugated Macrocycles. Part XXXI.* Catalytic Hydrogenation of Tetrazaporphins, with a Note on its Stereochemical Course.†*

By G. E. FICKEN, R. P. LINSTEAD, EDITH STEPHEN, and MARGARET WHALLEY.

Hydrogenation of tetrazaporphins in the presence of very active catalysts gave substances easily decomposed to the imides of dibasic acids. With palladium black as catalyst, tetrazaporphin (I; R = R′ = H) and three of its alkyl derivatives gave reasonably stable, coloured tetrahydro-derivatives. The hydrogenation level of these substances was established by degradation to saturated imides, by quantitative dehydrogenation, and by spectral evidence.

The dehydrogenation of tetra*cyclo*hexenotetrazaporphin (I; RR′ = $-[CH_2]_4-$) with quinones is described.

CATALYTIC hydrogenation of tetrazaporphin [1] (I; R = R′ = H) (now more accessible because of an improved method for preparation of maleinitrile [2]), of its tetramethyl [3] (I; R = H, R′ = Me), octamethyl [4] (I; R = R′ = Me), and tetra*cyclo*hexeno- [5] (I; RR′ = $-[CH_2]_4-$) derivatives and of the corresponding magnesium complexes (II) has been



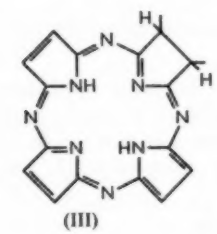
investigated. The metal-free pigments in pyridine, chlorobenzene, or 2-ethoxyethanol and the magnesium pigments in pyridine were rapidly destroyed over active catalysts such as Adams platinum oxide or W-4 Raney nickel. It seems likely that hydrogenation at

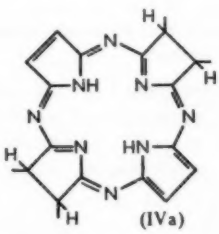
* Part XXX, *J.*, 1957, 2882.
† A preliminary account appeared in Special Publication No. 3, The Chemical Society, 1955, p. 98.
[1] Linstead and Whalley, *J.*, 1952, 4839.
[2] Woods, Imperial Chemical Industries Limited, personal communication; cf. U.S.P. 2,447,810/1948.
[3] Brown, Spiers, and Whalley, *J.*, 1957, 2882.
[4] Baguley, France, Linstead, and Whalley, *J.*, 1955, 3521.
[5] Ficken and Linstead, *J.*, 1952, 4846.

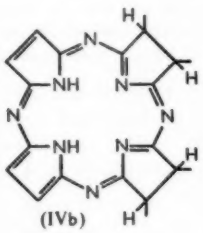
the β-positions of the pyrrole rings is accompanied by hydrogenolysis of the macrocycle, the linear, possibly polypyrrolic, intermediates then being hydrolysed. The only products isolated from the magnesium complexes of tetramethyl-, octamethyl-, and tetra*cyclo*hexeno-tetrazaporphin were saturated imides, *viz.*, methylsuccinimide, αα′-dimethylsuccinimide, and *cis*-hexahydrophthalimide. Under similar conditions phthalimide was obtained from magnesium and zinc phthalocyanine.[6]

Controlled hydrogenation was possible by using palladium black.[7] With the metal-free pigments hydrogenation was slow and considerable loss was caused by over-hydrogenation. With the more soluble magnesium pigments in pyridine, preparative hydrogenation was practicable. The magnesium derivatives of tetramethyl-, octamethyl-, and tetra*cyclo*hexeno-tetrazaporphin gave, after 2 mols. of hydrogen had been absorbed, royal-blue solutions which did not show the strong visible and ultraviolet fluorescence characteristic of the parent pigments. The spectra of the blue solutions were of the metal-tetrazaporphin type: in each case hydrogen caused a bathochromic shift of *ca.* 30 mμ in the position of the longest-wavelength band. The blue pigments, either solid or in solution, were readily oxidised in air, to the starting materials contaminated with traces of unidentified pigments which absorbed at longer wavelength (663, 665, and 666 mμ severally). Under the same conditions, hydrogenation of magnesium tetrazaporphin (II; R = R′ = H) gave very small yields of a blue pigment ($\lambda_{max.}$ 608, 454 mμ in pyridine) which was rather more stable to atmospheric oxidation. Magnesium phthalocyanine in dilute solution in pyridine slowly formed a blue pigment ($\lambda_{max.}$ 709, 570 mμ) which in air gave instant and quantitative recovery of magnesium phthalocyanine.

In acetic acid the reduced magnesium pigments from tetramethyl-, octamethyl-, and tetra*cyclo*hexeno-tetrazaporphin gave purple microcrystalline, sparingly soluble (6—8 mg./100 c.c. of chlorobenzene) metal-free compounds. These pigments were reasonably


(III)


(IVa)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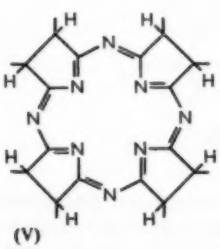
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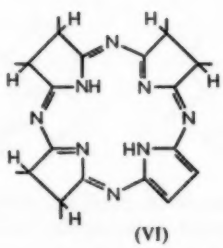
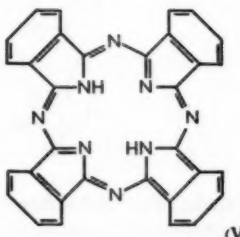

(VI)


(VII)

stable to oxidation at room temperature but in boiling chlorobenzene or, better, chlorobenzene–nitrobenzene they oxidised to the parent pigment: this made purification by crystallisation impracticable. The number and position of the " extra " hydrogen atoms in these compounds was still to be determined.

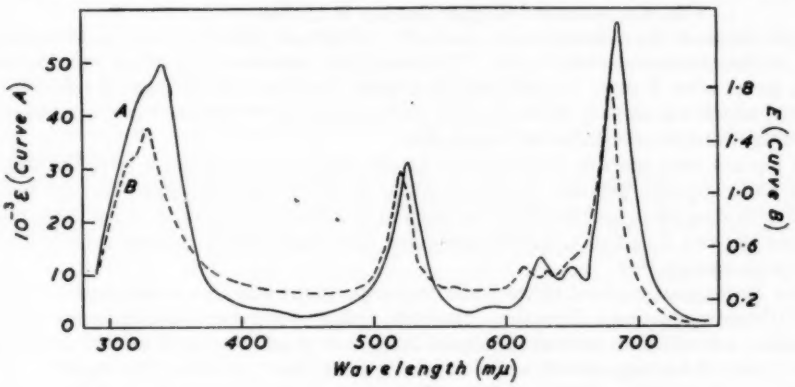
Several coloured hydrotetrazaporphins with the β-positions of one or more pyrrolic

[6] Barrett, Dent, and Linstead, *J.*, 1936, 1719.
[7] Wieland, *Ber.*, 1912, **45**, 489.

corners reduced, are formally possible. The dihydro-form (III) corresponds to the relatively stable chlorin [8] in the porphyrin series. The tetrahydro-compound may be formulated as (IVa) (corresponding to bacteriochlorophyll [9]) or (IVb). Formulæ (V) and (VI) represent possible hexahydro-forms. In (II), (III), (IV), and (V) a large conjugated ring is retained [in (V) by transfer of 2 hydrogen atoms from central nitrogen atoms to β-pyrrolic carbon atoms]. In the hexahydro-compound (VI) the conjugation of the large ring is interrupted.

The more obvious methods for deciding between the possible structures proved unhelpful. Hydrogen uptake figures suggested a tetrahydro-structure for the magnesium hydrotetrazaporphins. This made structure (V) or (VI) unlikely for the metal-free pigments. It was, however, uncertain whether the metal-free pigments were at the tetrahydro- or the dihydro-level because of the possibility of partial dehydrogenation during demetallation. Carbon and hydrogen determinations on the metal-free pigments were inconclusive.

Spectra of (A) tetrahydro-octamethyltetrazaporphin and (B) tetrahydrotetrazaporphin in chlorobenzene.



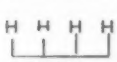
Vigorous oxidation of a symmetrically substituted tetrazaporphin (cf. refs. 3, 4, 5) yields 4 mols. of the corresponding unsaturated imide. The dihydro-derivative (III) and the tetrahydro-compound (IVa or b) would therefore be expected to yield 1 mol. and 2 mols. of saturated imide respectively. In fact oxidation of hydro-octamethyltetrazaporphin gave αα′-dimethylsuccinimide (0·95 mol.) and dimethylmaleimide (1·77 mols.). Allowing for the (determined) experimental loss the yield of saturated imide becomes 1·19 mols. This still takes no account of the loss (unknown) through dehydrogenation of the pigment before ring scission. It is clear that the true yield of saturated imide is more than 1 mol. and therefore that the hydro-pigment contains more than one reduced pyrrolic corner. The hydro-pigment must therefore be at the tetrahydro-level since a higher level was excluded. This was confirmed by the results of quantitative dehydrogenation described below.

Similar oxidation of hydrotetra*cyclo*hexenotetrazaporphin and of hydrotetramethyltetrazaporphin gave *cis*-hexahydrophthalimide (0·3 mol.) and methylsuccinimide (0·4 mol.). The low yields of saturated imide in these two cases is not unexpected because of the greater ease of dehydrogenation of these hydrogenation products which would greatly increase the extent of dehydrogenation before ring scission. However, the absorption spectra of hydrotetra*cyclo*hexenotetrazaporphin, hydro-octamethyltetrazaporphin and hydrotetrazaporphin ($\lambda_{max.}$ 678, 525 mμ in chlorobenzene; obtained in minute yield from

[8] Cf., *e.g.*, Eisner and Linstead, *J.*, 1955, 3742.
[9] Golden, Linstead, and Whitham, *J.*, 1958, 1725.

magnesium tetrazaporphin) resemble so closely that of tetrahydro-octamethyltetrazaporphin (see Figure) that they too must be tetrahydro-derivatives.

The isolation of succinimide derivatives by degradation of the hydrotetrazaporphins indicated that the extra hydrogen atoms were on the β-positions of two of the pyrrolic corners of the macrocycles. It is of special interest that the αα′-dimethylsuccinimide from tetrahydro-octamethyltetrazaprophin was isolated in the *unstable meso*-form [10] in which the hydrogen atoms are *cis*- with respect to the imide ring. This shows that, as in the mild catalytic hydrogenation of polynuclear aromatic compounds,[11] there is one-sided addition of hydrogen to the molecule. This in turn would correspond with addition to each double bond of both atoms of hydrogen during one period of sorption on the catalyst. There is no evidence from measurements of light absorption during hydrogenation (or during dehydrogenation with air, boiling nitrobenzene, dilute nitric acid, or quinones) for the formation of a dihydro-pigment. If it may be presumed from this that all four atoms of hydrogen are added during a single period of sorption, it may be concluded that the tetrahydride is not only *cis* but *cis-syn-cis*, to apply the nomenclature used [12] for the hydrides of polynuclear aromatic compounds. This is represented diagramatically in (VIII).



(VIII)

Indications of the existence of a hexahydro-compound (possibly V or VI) were obtained only in the tetra*cyclo*hexeno-series. The metal-free pigment in pyridine over palladium black gave, after 3 mols. of hydrogen had been absorbed, an olive-green solution ($\lambda_{max.}$ 720 mμ) which was rapidly oxidised in air (with uptake of 0·5 mol. of oxygen) to a solution of tetrahydrotetra*cyclo*hexenotetrazaporphin.

It has not been possible to determine, as yet, whether our products have the structure (IVa) with opposite pyrrolic corners reduced or (IVb) with adjacent corners reduced. The simple absorption spectra, however, suggest that they are not mixtures of the two forms because the two forms of tetrahydroporphins have been shown to have widely differing absorption spectra.[13,14]

The hydrogenation level of the hydrotetrazaporphins was also established by quantitative dehydrogenation. Titration methods using potassium dichromate, hydrogen peroxide, or ferric alum were unsuccessful because ring scission accompanied dehydrogenation; but dehydrogenation with quinones, a method successfully applied to the dehydrogenation of synthetic chlorins,[15] confirmed the tetrahydro-structure for our products: hydro-octamethyltetrazaporphin in *o*-dichlorobenzene at room temperature was 50% dehydrogenated by 1 mol. of 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone and 100% dehydrogenated by 2 mols. The product was octamethyltetrazaporphin which was spectroscopically identical with the pigment prepared from dimethylfumaronitrile.[4] The isolation of 2 : 3-dichloro-5 : 6-dicyanoquinol from the reaction indicated that transfer of the " extra " hydrogen atoms to the quinone had in fact occurred. With quinones of lower potential, *e.g.*, tetrachloro-1 : 2-benzoquinone and chloranil, dehydrogenation was slow at 80° and was accompanied by thermal decomposition of both pigment and quinone.

Dehydrogenation of tetrahydrotetra*cyclo*hexenotetrazaporphin with an excess of chloranil at 110° gave nearly complete conversion into the parent pigment (II; RR′ = $-[CH_2]_4-$). With an excess of 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone at 80°, the tetrahydro-pigment gave initially the parent tetrazaporphin but then the *cyclo*hexene rings were successively dehydrogenated to yield, finally, phthalocyanine (VII). Two of the intermediate pigments—benzotri*cyclo*hexeno- ($\lambda_{max.}$ 647, 571 mμ) and tribenzo*cyclo*hexeno-tetrazaporphin ($\lambda_{max.}$ 680, 610 mμ)—were identified by comparison of the absorption

[10] Linstead and Whalley, *J.*, 1954, 3722.
[11] Linstead, Doering, Davis, Levine, and Whetstone, severally, *J. Amer. Chem. Soc.*, 1942, **64**, 1985—2022.
[12] *Idem, ibid.*, p. 1985.
[13] Dorough and Miller, *J. Amer. Chem. Soc.*, 1952, **74**, 6106.
[14] Barnard and Jackman, *J.*, 1956, 1174.
[15] Eisner and Linstead, *J.*, 1955, 3749; Eisner, Linstead, Parkes, and Stephen, *J.*, 1956, 1655.

maxima with those of the known pigments.[16] The third intermediate ($\lambda_{max.}$ 671, 585 mμ) was spectroscopically identical with the pigment obtained by treatment of tetra*cyclo*hexenotetrazaporphin with 6 mols. of dichlorodicyanobenzoquinone at 110° or with an excess of tetrachloro-1 : 2-benzoquinone at 80°. The spectrum and elementary analysis of this pigment suggest that it is dibenzodi*cyclo*hexenotetrazaporphin. Quinones of lower potential, such as 9 : 10-anthraquinone and duroquinone, failed to remove the "extra" hydrogen atoms from tetrahydrotetra*cyclo*hexenotetrazaporphin. The progressive dehydrogenation of the hydro-derivatives of phthalocyanine can be represented in the following scheme where the numbers refer to the extra hydrogen atoms on the four *iso*indole rings: 6.4.6.4 ⟶ 4.4.4.4 ⟶ 4.4.4.0 ⟶ 4.0.4.0 ⟶ 4.0.0.0 ⟶ 0.0.0.0.

Experimental

Microanalyses were carried out in the Microanalytical Laboratory (Mr. F. H. Oliver and Miss J. Cuckney) of this Department.

Maleinitrile.[2]—Fumaronitrile [17] (8·5 g.) was heated with iodine (0·5 g.) at 175—180° for 6·5 hr. The product was dissolved in chloroform (120 c.c.). Sodium thiosulphate (5 g.) was added and the mixture was kept overnight. The chloroform solution was decanted, and the residue was distilled to give fumaronitrile, b. p. 90—95/20 mm. (5·4 g.), and maleinitrile, b. p. 110—120°/20 mm. (2·75 g., 89% on unrecovered fumaronitrile).

Pyridine for Hydrogenations.—Pyridine (from Messrs. Hopkin and Williams, "pure") (500 c.c.) was refluxed for 4 hr. with W-4 Raney nickel (1 teaspoonful) and then redistilled from fresh Raney nickel.

*Tetrahydrotetra*cyclo*hexenotetrazaporphin.*—(i) A suspension of magnesium tetra*cyclo*hexenotetrazaporphin monohydrate monopyridine solvate [5] (222 mg.) in pyridine (100 c.c.) was hydrogenated over palladium black [7] (53 mg.) until 2 mols. of hydrogen had been absorbed. The solution was filtered rapidly under nitrogen and the pyridine was removed under reduced pressure (no air-leak). Filtered acetic acid (20 c.c.) was added and the mixture was kept at room temperature under reduced pressure for 2 hr. Filtered, distilled water was added. *Tetrahydrotetra*cyclo*hexenotetrazaporphin* (140 mg., 76%) separated as a dark purple powder (Found: C, 72·1; H, 6·9; N, 20·8. $C_{32}H_{36}N_8$ requires C, 71·9; H, 7·2; N, 21·0%). (ii) Tetra*cyclo*hexenotetrazaporphin (264 mg.) was suspended in pyridine (50 c.c.) and hydrogenated over palladium black for 7 days: 2·93 mols. of hydrogen were absorbed. The olive-green solution was shaken with air: 0·94 atom of oxygen was absorbed. The purple solution was decanted from the palladium black into 2N-hydrochloric acid (100 c.c.). Tetrahydrotetra*cyclo*hexenotetrazaporphin (217 mg., 82%) spectroscopically identical with that prepared from the magnesium pigment was obtained.

Tetrahydro-octamethyltetrazaporphin.—Magnesium octamethyltetrazaporphin monopentanolate [4] (250 mg.) was hydrogenated in pyridine (100 c.c.) over palladium black (19 mg.). 2·0 Mols. of hydrogen were absorbed. The solution was filtered rapidly and the pyridine was removed under reduced pressure (no air-leak). Acetic acid (20 c.c.) was added, followed, after 2 hr., by water (20 c.c.). *Tetrahydro-octamethyltetrazaporphin* (159 mg., 84%) was precipitated as a purple solid (Found: C, 67·2; H, 6·7; N, 26·3. Calc. for $C_{34}H_{30}N_8$: C, 66·9; H, 7·0; N, 26·0%). The pigment in chlorobenzene passed down kieselguhr or tartaric acid columns as a single band. Alumina caused dehyrogenation to the ground-level pigment.

Tetrahydrotetramethyltetrazaporphin.—This experiment must be completed within 6 hr. Magnesium tetramethyltetrazaporphin monomethanolate [3] (210 mg.) was hydrogenated in pyridine (100 c.c.) over palladium black (55 mg.). The solution became brown and then light green (*ca.* 2 hr.). The reaction was then stopped and the mixture was filtered rapidly under nitrogen. The royal-blue filtrate was evaporated to dryness under reduced pressure and cold acetic acid (20 c.c.) was added to the ice-cold residue. After 2 hr. the acetic acid was removed under reduced pressure and water (20 c.c.) was added. *Tetrahydrotetramethyltetrazaporphin monohydrate* (83 mg., 43%) was obtained as a dark purple solid after drying (room temperature/0·01 mm.) (Found: C, 61·8; H, 5·9; N, 29·1. $C_{20}H_{24}N_8O$ requires C, 61·2; H,

[16] Brown, Linstead, and Whalley, unpublished work.
[17] *Org. Synth.*, **30**, 46.

6·1; N, 28·6%). Drying the pigment at slightly higher temperatures invariably caused dehydrogenation to tetramethyltetrazaporphin.

Oxidation of Tetrahydro-octamethyltetrazaporphin.—The pigment (287 mg.) was dissolved in concentrated sulphuric acid (5 c.c.) at −5° under nitrogen. 0·01N-Potassium dichromate (100 c.c.) was added all at once. After 2 min. ferrous sulphate (3 g.) was added and the solution was filtered to remove octamethyltetrazaporphin ($\lambda_{max.}$ in chlorobenzene 627, 556 mμ) (9 mg., 3%). The filtrate was extracted continuously with ether for 48 hr. The extract was concentrated to *ca.* 10 c.c. (inversion of configuration occurs if the ether extract is evaporated to dryness at this stage or during extraction) and the solution was chromatographed on silica gel loaded with water.[18] The column was eluted with ether. Twenty-four 4-c.c. fractions were collected. Fractions 1—6 yielded dimethylmaleimide (136 mg., 1·7 mols.), m. p. 117—119°, fractions 7 and 8 gave a mixture (6 mg.) and fractions 9—23 contained *meso*-αα′-dimethylsuccinimide (78 mg., 0·95 mol.), m. p. and mixed m. p. 43—45°.[8]

Oxidation and separation as described above of dimethylmaleimide (95 mg.) and dimethylsuccinimide (99 mg.) gave 75 mg. (79% recovery) of the former and 79 mg. (80% recovery) of the latter and 4 mg. of a mixture.

Oxidation of Tetrahydrotetracyclohexenotetrazaporphin.—The pigment (305 mg.) was oxidised as described above. The ether extract was evaporated to dryness, the residue was dissolved in wet benzene, and the solution was chromatographed on silica gel.[18] Fractions 1—17 yielded 3 : 4 : 5 : 6-tetrahydrophthalimide (198 mg., 2·3 mol.), m. p. and mixed m. p. 169—172°, and *cis*-hexahydrophthalimide [19] (27 mg., 0·3 mol.), m. p. and mixed m. p. 133—137°.

Oxidation of Tetrahydrotetramethyltetrazaporphin.—The pigment monohydrate (165 mg.) was dissolved in concentrated sulphuric acid (4 c.c.) at 0° under nitrogen and chromium trioxide (100 mg.) was added in a little water. The mixture was kept at room temperature for 5 min. and excess of ferrous sulphate was then added. The solution was continuously extracted with ether overnight and the extract was chromatographed on silica gel [18] as above. Fractions 1—7 contained citraconimide (69 mg., 1·5 mols.), fractions 8—10 contained no solute, and fractions 11—15 yielded methylsuccinimide (20 mg., 0·4 mol.), m. p. and mixed m. p. 61—64°.

Hydrogenation of Magnesium Phthalocyanine Monohydrate.—Crude magnesium phthalocyanine [6] was crystallised several times from pyridine to give the purple monohydrate (Found: C, 68·7; H, 3·7; N, 19·9; Mg, 4·5. Calc. for $C_{32}H_{16}N_8Mg,H_2O$: C, 69·2; H, 3·3; N, 20·2; Mg, 4·4%). A solution of the pigment in pyridine (0·34 mg./100 c.c.; 20 c.c.) was hydrogenated over palladium black for 16 hr. The blue solution was shaken in the air and immediately reoxidised to a solution of magnesium phthalocyanine (0·34 mg./100 c.c., estimated spectroscopically from the absorption at 674 mμ).

Exhaustive Hydrogenations.—(i) Magnesium tetra*cyclo*hexenotetrazaporphin monohydrate monopyridine solvate (350 mg.) was hydrogenated in pyridine (50 c.c.) over Adams platinum oxide (50 mg.) until no more hydrogen was absorbed. The pyridine was removed under reduced pressure and the dark sticky residue was extracted with light petroleum (b. p. 60—80°). *cis*-Hexahydrophthalimide (21 mg., 0·25 mol.), m. p. and mixed m. p. 133—135°, separated.

(ii) Magnesium octamethyltetrazaporphin monopentanolate (237 mg.) was hydrogenated in pyridine (35 c.c.) over Adams platinum oxide for 3 days. The dark green solution was filtered through charcoal and the filtrate was evaporated to dryness under reduced pressure. The residue was sublimed and the sublimate was crystallised from water to give DL-αα′-dimethylsuccinimide (21 mg., 0·38 mol.), m. p. 99—101°, mixed m. p. 101—102° [8] (no precautions were taken to prevent possible inversion of configuration of the primary product).

(iii) Magnesium phthalocyanine monohydrate (97 mg.) was hydrogenated in pyridine (50 c.c.) over Adams platinum oxide (23 mg.) for 6 days. 11·5 Mols. of hydrogen were absorbed. The brown mixture was shaken with air; magnesium phthalocyanine (6% of the original quantity, estimated spectroscopically) was re-formed. The solution was filtered and the filtrate was evaporated to dryness at room temperature. The residual solid was extracted with light petroleum (b. p. 60—80°), and the extract was evaporated to dryness. Sublimation of the residue gave phthalimide (53 mg., 2·1 mols.), m. p. 224—226° and 229—232° after further sublimation.

(iv) Zinc phthalocyanine monopyridine solvate [4] (188 mg.) was hydrogenated as above.

[18] Elvidge, Linstead, and Whalley, "Modern Techniques of Organic Chemistry," Butterworths, London, 1955, p. 9.
[19] Ficken and Linstead, *J.*, 1954, 3730.

10 Mols. of hydrogen were absorbed. The brown solution was filtered through charcoal, and the filtrate was evaporated to dryness under reduced pressure. The solid was dissolved in a little ethanol and the solution was diluted with benzene (4 vols.). The solution was chromatographed on alumina (Spence H) and gave (*a*) a weakly adsorbed green band containing a trace of zinc phthalocyanine, (*b*) a yellow band which yielded phthalimide (97 mg., 2·1 mols.), m. p. 229—231°, and (*c*) a strongly adsorbed rose-pink band which was eluted with 50% aqueous pyridine and gave no identifiable product.

Dehydrogenation of Tetrahydro-octamethyltetrazaporphin.—(i) The following control experiments showed that Beer's law is obeyed by mixtures of octamethyltetrazaporphin (A) and tetrahydro-octamethyltetrazaporphin (B) in *o*-dichlorobenzene.

	530 mμ		560 mμ		630 mμ		685 mμ	
Concn. (mg./100 c.c.)	$E_{obs.}$	$E_{calc.}$	$E_{obs.}$	$E_{calc.}$	$E_{obs.}$	$E_{calc.}$	$E_{obs.}$	$E_{calc.}$
A 0·2295, B 0·2282	0·232	0·231	0·232	0·235	0·391	0·413	0·416	0·422
A 0·1148, B 0·3400	0·262	0·276	0·121	0·131	0·251	0·252	0·630	0·637
A 0·3440, B 0·1157	0·180	0·189	0·314	0·318	0·540	0·522	0·209	0·213

It was also shown that solutions of octamethyltetrazaporphin and of tetrahydro-octamethyltetrazaporphin in *o*-dichlorobenzene were essentially unchanged after 4 hr. at 80° under nitrogen.

Method A. 5-C.c. portions of a solution of tetrahydro-octamethyltetrazaporphin (2—3 mg./100 c.c. of *o*-dichlorobenzene) were treated with varying molar proportions of 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone (11—12 mg. in 25 c.c. of *o*-dichlorobenzene) at 80° for 2·75 hr. (apparatus [20]). Each solution was then withdrawn with a long-necked pipette and the flask was rinsed several times with *o*-dichlorobenzene. The combined solution and washings were made up to 25 c.c. and the resulting solution was examined spectrophotometrically at 530, 560, 630, and 685 mμ.

Method B. 1-C.c. portions of a solution of tetrahydro-octamethyltetrazaporphin (3·4 mg./100 c.c. of dry *o*-dichlorobenzene) were placed in ampoules. To each was added a solution of 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone (11·2 mg./100 c.c. of dry *o*-dichlorobenzene: 0·5—2·0 mols.). The ampoules were sealed and kept in the dark at room temperature for 22 hr. The solutions were then made up to 10·0 c.c. with *o*-dichlorobenzene and each was examined spectrophotometrically at 530, 560, 630, and 685 mμ.

Quinone (mols.)	Unchanged hydro-deriv. (%)		Dehydrogenated pigment (%)		Dehydrogn. (%)
	530 mμ	685 mμ	560 mμ	630 mμ	
	Method A				
0·5	77	70	34	32	30
1·0	52	49	49	50	50
1·4	33	32	62	67	67
2·0	6	8	95	97	95

Quinone (mols.)	Unchanged hydro-deriv. (%)		Dehydrogenated pigment (%)		Dehydrogn. (%)
	530 mμ	685 mμ	560 mμ	630 mμ	
	Method B				
0·5	—	70	26	26	27
1·0	—	44	47	50	52
1·25	35	33	60	59	62
1·5	24	29	70	70	72
2·0	3	10	91	94	93

The results tabulated above are each the average of two or more independent experiments.

(ii) Tetrahydro-octamethyltetrazaporphin (14·4 mg.) was heated with 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone (180 mg., 3 mols.) in dry *o*-dichlorobenzene (100 c.c.) in the dark for 17 hr. at 80°. The solution was evaporated to small bulk and octamethyltetrazaporphin (13·7 mg., 95%) then separated. It was washed with ether and twice crystallised extractively from *o*-dichlorobenzene (Found: 560 mμ, log ε 4·58; 630 mμ, log ε 4·78. Octamethyltetrazaporphin has log ε 4·58 and 4·78 respectively). The combined filtrate and washings were evaporated and gave 2 : 3-dichloro-5 : 6-dicyanoquinol (10 mg., 55%), m. p. and mixed m. p. 257—259° (Thiele and Gunter [21] give 265°). The product gave the pink colour characteristic for the quinol with aqueous ferric chloride.

[20] Braude, Jackman, and Linstead, *J.*, 1954, 3548.
[21] Thiele and Gunter, *Annalen*, 1906, **349**, 54.

Dehydrogenation of Tetracyclohexenotetrazaporphin and its Derivatives.—(i) A solution of tetra*cyclo*hexenotetrazaporphin or of tetrahydrotetra*cyclo*hexenotetrazaporphin in *o*-dichlorobenzene was boiled with a large excess of 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone. Phthalocyanine ($\lambda_{max.}$ 698, 665 mμ) was the only pigment produced.

(ii) Tetra*cyclo*hexenotetrazaporphin (1 mol.) in *o*-dichlorobenzene was heated at 110° with dichlorodicyanobenzoquinone (6 mols.) for 17 hr. in a sealed ampoule. The product was dibenzodi*cyclo*hexenotetrazaporphin ($\lambda_{max.}$ 671, 584 mμ) containing traces of benzotri*cyclo*hexenotetrazaporphin [21] ($\lambda_{max.}$ 647, 571 mμ) and unchanged starting material.

(iii) Tetra*cyclo*hexenotetrazaporphin in chlorobenzene was heated with an excess of tetrachloro-1 : 2-benzoquinone at 80° for 2 days. The solution was diluted and was then chromatographed (alumina, Spence H). Three pigments were eluted with chlorobenzene, *viz.*, (i) blue ($\lambda_{max.}$ 647, 571 mμ), monobenzotri*cyclo*hexenotetrazaporphin [16] (traces), (ii) violet ($\lambda_{max.}$ 671, 586 mμ) main product, and (iii) blue-green ($\lambda_{max.}$ 680, 615 mμ), tribenzo*cyclo*hexenotetrazaporphin [21] (traces). The violet fraction was concentrated and rechromatographed, to give the violet pigment contaminated with traces of the monobenzo-compound. Repeated extractive crystallisation of the pigment from benzene gave dark blue needles of *dibenzodicyclohexenotetrazaporphin* (Found: C, 72·8; H, 5·1. $C_{32}H_{26}N_8$ requires C, 73·5; H, 5·0%).

(iv) Dibenzodi*cyclo*hexenotetrazaporphin and benzotri*cyclo*hexenotetrazaporphin in *o*-dichlorobenzene with a large excess of dichlorodicyanobenzoquinone at 150° each gave tribenzo*cyclo*hexenotetrazaporphin ($\lambda_{max.}$ 680, 610 mμ) and phthalocyanine.

Absorption Spectra.—For qualitative work a Hilger–Nutting spectrophotometer and a Hartridge reversion spectroscope were used. Quantitative spectra were obtained on a Unicam S.P. 500 (250—400 mμ) and a S.P. 600 (400—1000 mμ) instrument. A reduced pigment (*ca.* 0·5 mg.) was dissolved in the solvent (100 c.c.) at room temperature and intensity measurements were completed within 1 hr.

Absorption spectra (mμ) *and* log ε.

Tetrazaporphin	Solvent						
Tetrahydro-octamethyl	PhCl	333	342	526	626	651	687	
		4·65	4·69	4·48	4·12	4·06	4·75	
	$C_6H_4Cl_2$	331	346	528	625	650	687	
		4·62	4·66	4·57	3·98	4·07	4·78	
Tetrahydrotetra*cyclo*hexeno...	$CHCl_3$	265	328	343	532	628	653	691
		4·03	4·69	4·76	4·45	4·23	4·11	4·78
Tetrahydrotetramethyl	PhCl	333	338	526	624	681		
		4·64	4·65	4·29	4·10	4·61		
Octamethyl	$C_6H_4Cl_2$	343	558	630				
		4·82	4·61	4·82				
Dibenzodi*cyclo*hexeno	$C_6H_4Cl_2$	346	544	586	671			
		4·78	4·31	4·91	4·83			
Magnesium phthalocyanine ...	C_5H_5N	347	568	587	610	647	674	
		4·73	3·59	3·79	4·45	4·39	4·94	

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790. *Synthesis of the 3-2′-Aminopropyl- and 3-2′-Aminobutyl-derivatives of 5-Hydroxyindole, and an Alternative Synthesis of 5-Hydroxytryptamine.**

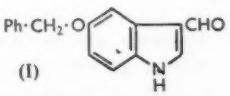
By A. S. F. Ash and W. R. Wragg.

5-Benzyloxy-3-formylindole (I), prepared from 5-benzyloxyindole, was condensed with nitromethane, nitroethane, and 1-nitropropane to give the respective 5-benzyloxy-3-2′-nitroalkenylindoles (III; R = C_6H_5·CH_2·O, R′ = H, Me, or Et). The corresponding 5-hydroxytryptamines were then prepared by reduction with lithium aluminium hydride followed by catalytic debenzylation. α-Methyltryptamine was similarly synthesised from 3-formylindole.

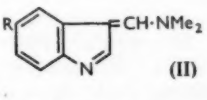
5-Benzyloxy-α-ethyltryptamine was also prepared by a less satisfactory route from 5-benzyloxygramine.

Boehme's synthesis [1] of 5-benzyloxyindole has been improved.

Although the true physiological significance of 5-hydroxytryptamine remains unknown,[2] interesting pharmacological properties may be expected in congeners of this compound, particularly since it may be a neurohormone.[3] We decided to synthesise the α-methyl and α-ethyl derivatives because of their analogy to amphetamine. Moreover, it seemed possible that these substituents might inhibit attack by amine oxidase, which apparently initiates the normal metabolic degradation of 5-hydroxytryptamine to 5-hydroxy-3-indolylacetic acid.[4]



(I)



(II)

In the more practicable of the two routes to α-alkyl-5-hydroxytryptamines examined in this work, the key intermediate was 5-benzyloxy-3-formylindole (I). This was prepared by treating 5-benzyloxyindole with dimethylformamide and phosphorus oxychloride, a known method for formylating indole itself.[5,6] The initial product, presumably a salt of 5-benzyloxy-3-dimethylaminomethyleneindolenine (II; R = Ph·CH_2·O), was hydrolysed to the aldehyde by dilute sodium carbonate solution. The unexpectedly low solubility of the aldehyde (I) in common solvents led us to enquire into its structure.

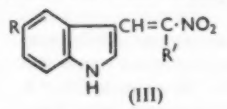
Molecular-weight determination confirmed that it was a monomer. Attempts to isolate the intermediate indolenine base (II; R = Ph·CH_2·O) at −5° gave only the aldehyde. By contrast, we were able to repeat the work of Smith [6] who had no difficulty in isolating the corresponding unsubstituted indolenine base (II; R = H) under similar conditions. The aldehyde evidently had an indole structure since the ultraviolet spectrum of a solution in dioxan resembled that of indole and of 5-benzyloxyindole, in which the main peaks were all below 300 mμ. In particular it lacked the strong peak at 355 mμ which characterised the indolenine (II; R = H). The infrared spectrum of the aldehyde (I) and of 3-formylindole contained the expected strong carbonyl band.

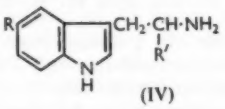
The aldehyde (I) was condensed with nitroethane and 1-nitropropane by refluxing it in an excess of the nitroalkane in the presence of benzylamine, the catalyst selected in model experiments (see below). The products, 5-benzyloxy-3-2′-nitropropenyl- and -3-2′-nitrobutenyl-indole (III; R = Ph·CH_2·O, R′ = Me and Et), obtained in yields of 60—80%, were reduced with lithium aluminium hydride in 40—50% yields to the corresponding

* Part of this work is the subject of B.P. Appl. No. 33141/55.

[1] Boehme, *J. Amer. Chem. Soc.*, 1953, **75**, 2502.
[2] Udenfriend, Shore, Bogdanski, Weissbach, and Brodie, *Recent Progr. Hormone Res.*, 1957, **12**, 1.
[3] Woolley and Shaw, *Proc. Nat. Acad. Sci. U.S.A.*, 1954, **40**, 228; Himwich, *Science*, 1958, **127**, 59.
[4] Sjoerdsma, Smith, Stevenson, and Udenfriend, *Proc. Soc. Exp. Biol. Med.*, 1955, **89**, 36.
[5] Tyson and Shaw, *J. Amer. Chem. Soc.*, 1952, **74**, 2273.
[6] Smith, *J.*, 1954, 3842.

α-alkyltryptamines (IV; R = Ph·CH_2·O, R′ = Me and Et). In these reductions a neutral by-product was formed, in spite of the use of an excess of lithium aluminium hydride: the infrared spectrum, analytical data, and neutral character indicated that it was 5-benzyloxy-3-hydroxymethylindole (V).


(III)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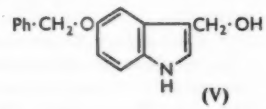
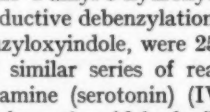
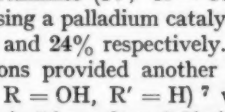
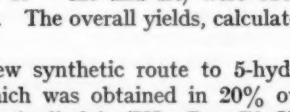

(V)

The α-alkyl-5-hydroxytryptamines (IV; R = OH, R′ = Me and Et) were obtained by reductive debenzylation, using a palladium catalyst. The overall yields, calculated on 5-benzyloxyindole, were 25% and 24% respectively.

A similar series of reactions provided another new synthetic route to 5-hydroxytryptamine (serotonin) (IV; R = OH, R′ = H) [7] which was obtained in 20% overall yield from the aldehyde (I), *via* 5-benzyloxy-3-2′-nitrovinylindole (III; R = Ph·CH_2·O, R′ = H) and 5-benzyloxytryptamine (IV; R = Ph·CH_2·O, R′ = H). This yield could no doubt be improved if the synthesis were studied in greater detail.


(VI)


(VII)


(VIII)

The other route to α-alkyl-5-hydroxytryptamines examined was condensation of 5-benzyloxygramine [8] (VI; R = Ph·CH_2·O) with a nitroalkane and reduction of the resultant nitroalkylindoles (VII; R = Ph·CH_2·O, R′ = H, R″ = Me and Et). In the preparation of unsubstituted α-alkyltryptamines, Snyder and Katz [9] found that 1- and 2-nitropropane condensed with gramine (VI; R = H), in the presence of sodium hydroxide, to give the corresponding nitroalkylindoles (VII; R = R′ = H, R″ = Et and R = H, R′ = R″ = Me) but nitromethane, nitroethane, and ethyl nitroacetate gave mainly bis-substituted products of type (VIII; R = H, R″ = H, Me, and CO_2Et). Without sodium hydroxide, ethyl nitroacetate was, however, only monoalkylated by gramine.[10]

We found that treatment of 5-benzyloxygramine (VI; R = Ph·CH_2·O) with nitroethane resulted mainly in dialkylation, even in the absence of added catalyst. Although a little of the required 5-benzyloxy-3-2′-nitropropylindole (VII; R = Ph·CH_2·O, R′ = H, R″ = Me) was isolated, this approach to 5-hydroxy-α-methyltryptamine was considered impracticable. 1-Nitropropane on the other hand gave a product which evidently consisted mainly of 5-benzyloxy-3-2′-nitrobutylindole (VII; R = Ph·CH_2·O, R′ = H, R″ = Et) because hydrogenation of the crude material, with Raney nickel, gave the desired α-alkyltryptamine (IV; R = Ph·CH_2·O, R′ = Et), isolated as the sulphate in 40% overall yield. The infrared spectrum of this sulphate was identical with that of the sample synthesised from 5-benzyloxy-3-formylindole (I).

Experiments to find suitable conditions for the condensation of 3-formylindoles with nitroalkanes led us to prepare α-methyltryptamine by a new route. 3-Formylindole failed to condense with nitroethane when the catalyst was (i) ethanolic potassium hydroxide, either at <0° or at reflux, (ii) alcoholic methylamine at room temperature, (iii) glacial acetic acid and sodium acetate, or (iv) acetic anhydride and sodium acetate, although similar conditions have been successfully employed in related nitrostyrene

[7] (*a*) Harley-Mason and Jackson, *J.*, 1954, 1165 and references cited therein; (*b*) Bernini, *Ann. Chim.* (*Italy*), 1953, **43**, 559; (*c*) Ek and Witkop, *J. Amer. Chem. Soc.*, 1954, **76**, 5579; (*d*) Speeter and Anthony, *ibid.*, p. 6209; (*e*) Justoni and Pessina, *Il Farmaco, Ed. Sc.*, 1955, **10**, 356.

[8] Kuhn and Stein, *Ber.*, 1937, **70**, 567.

[9] Snyder and Katz, *J. Amer. Chem. Soc.*, 1947, **69**, 3140.

[10] Lyttle and Weisblat, *ibid.*, p. 2118.

preparations.[7c,11] A little 3-2′-nitropropenylindole (III; R = H, R′ = Me) (9%) was formed in acetic acid in the presence of ammonium acetate, but a practicable yield (51%) was obtained only by the use of benzylamine as catalyst [12] and excess of refluxing nitroethane as solvent. These relatively drastic conditions contrast with the use of methylamine at room temperature for condensation of 3-formyl-2-methylindole with nitromethane.[13]

Reduction of the nitropropenyl compound (III; R = H, R′ = Me) by lithium aluminium hydride, followed by distillation of the basic product, gave a sample of 3-2′-aminopropylindole, the melting point of which was 97—98°, not depressed when mixed with a sample synthesised from gramine *via* 3-2′-bromopropylindole.[14] Snyder and Katz [9] have given a melting point of 80—81° for this base when prepared by reduction of 3-2′-nitropropylindole.

For the preparation of substantial quantities of 5-benzyloxyindole, Boehme's synthesis [1] of this compound from *p*-acetamidophenol was modified in several respects. First, in preparing the intermediate ethyl 5-benzyloxyindole-2-carboxylate, sodium acetate was used instead of sodium hydroxide for the condensation of diazotised *p*-benzyloxyaniline with ethyl methylacetoacetate.[15] This resulted in improved control of pH during the coupling reaction and ensured reproducible yields when the product was subsequently subjected to Fischer indole ring closure. Secondly, the decarboxylation of 5-benzyloxyindole-2-carboxylic acid was improved by using boiling quinoline as solvent and a copper chromite catalyst,[16] instead of heating the solid acid alone. The 5-benzyloxyindole so produced occasionally contained a brown impurity which was not eliminated by several recrystallisations, with charcoal, from benzene–light petroleum or carbon tetrachloride. A single rapid passage through a short column of alumina, with benzene and chloroform as eluants, readily removed the coloured material. Concentration of the eluate gave almost colourless 5-benzyloxyindole of the high quality which we find is required for the preparation of 5-benzyloxygramine in satisfactory and reproducible yield.

Experimental

M. p.s determined in evacuated capillaries are designated: m. p. (e.c). All other m. p.s were determined in open capillaries.

Ethyl 5-Benzyloxyindole-2-carboxylate.—Sodium nitrite (147 g.) in water (320 ml.) was run in below the surface of an ice-cooled, stirred suspension of *p*-benzyloxyaniline hydrochloride [1] (471 g.) and ice (1720 g.) in concentrated hydrochloric acid (621 ml.) and water (1240 ml.). The temperature fell to −5° to −10°. After 1 hour's stirring, acid-washed charcoal was added and the mixture filtered through "Hyflo Supercel." The filtrate was added all at once to a stirred suspension of ethyl methylacetoacetate (320 g.), sodium acetate (1640 g.), and ice (1440 g.) in ethanol (2920 ml.), and the mixture was stirred for 2 hr. When the mixture had warmed to room temperature after 2 hr., it was extracted with benzene (2 × 1500; 3 × 800 ml.). The extract was washed with water (400 ml.), dried ($MgSO_4$), and evaporated, leaving crude ethyl pyruvate *p*-benzyloxyphenylhydrazone as a red oil.

The phenylhydrazone was dissolved in ethanol (350 ml.) at 0°. Ethanol saturated at 0° with hydrogen chloride (1050 ml.) was rapidly added to the stirred solution, which then refluxed vigorously. A solid separated and the mixture was stirred without heating for 1 hr. After cooling in ice (½ hr.), the product was filtered off and washed with ice-cold ethanol (3 × 200 ml.) and hot water (3 × 500 ml.). Ethyl 5-benzyloxyindole-2-carboxylate was obtained as a yellow solid, m. p. 161—163° (352 g., 60%). Boehme [1] gives m. p. 110—117·5° (crude, yield 46—49%) and 162—164° (pure).

5-Benzyloxyindole.—A flask containing a stirred mixture of 5-benzyloxyindole-2-carboxylic

[11] Johnson and Hamilton, *J. Amer. Chem. Soc.*, 1941, **63**, 2864; Gairaud and Lappin, *J. Org. Chem.*, 1953, **18**, 1.
[12] Worrall, *J. Amer. Chem. Soc.*, 1934, **56**, 1556.
[13] Seka, *Ber.*, 1924, **57**, 1868.
[14] Dr. R. M. Jacob, personal communication.
[15] Dr. K. Gaimster, personal communication.
[16] Snyder and Beilfuss, *J. Amer. Chem. Soc.*, 1953, **75**, 4921.

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acid [1] (86 g.), freshly distilled quinoline (175 ml.), and copper chromite (0·9 g.) under nitrogen was immersed in a metal-bath at >200° and heated at 280° until carbon dioxide evolution was virtually complete (1½—2 hr.). The cooled brown syrup was poured into ether (900 ml.), stirred with charcoal, and filtered, and the filtrate extracted with 2N-hydrochloric acid (2 × 300; 2 × 200 ml.) and then with 2N-sodium hydroxide (2 × 200 ml.). The ether solution was washed with water (3 × 100 ml.), stirred with charcoal, and dried (Na_2SO_4). Removal of ether left an orange-yellow solid which was dissolved in hot carbon tetrachloride (500 ml.), boiled with charcoal, and filtered. 5-Benzyloxyindole separated as fawn needles, m. p. 99—101·5° (55·0 g., 77%).

Alternative Chromatographic Purification.—A solution of crude 5-benzyloxyindole (59·0 g.) in benzene (1 l.) was run on a column of alumina (15 cm. × 5 cm.) which was eluted with benzene (2 l.) and then with chloroform (3 l.). The combined eluates were evaporated, leaving an off-white solid (48·0 g.) which was crystallised from a mixture of benzene (250 ml.) and light petroleum (b. p. 60—80°; 1100 ml.) giving colourless or pale yellow needles, m. p. 100° (shrinks), 105—107° (44·0 g.) (Found: C, 80·5; H, 6·2; N, 6·0. Calc. for $C_{15}H_{13}ON$: C, 80·7; H, 5·9; N, 6·3%). Burton and Leong [17] give m. p. 107° and suggest that a m. p.[1, 18] of about 96° is that of a metastable form.

5-Benzyloxy-3-formylindole.—Phosphorus oxychloride (66·8 g., 0·44 mole) was added dropwise with stirring to excess of dimethylformamide (116 g.) in a flask protected from moisture, the internal temperature being kept at 10—20°. 5-Benzyloxyindole (98 g., 0·44 mole) in dimethylformamide (70 g.) was then slowly added with stirring, the temperature being kept at 15—25°. The temperature was then held at 35° (±2°) for 45 min. The mixture was poured on ice; a pale yellow solid separated, presumably a salt of 5-benzyloxy-3-2′-dimethylaminomethyleneindolenine. The solid was collected and then hydrolysed for 2 min. by boiling 2N-sodium carbonate (500 ml.). The suspension, which now smelt strongly of dimethylamine, was cooled in ice and the buff-coloured granular precipitate filtered off and washed successively with water (1750 ml.), ice-cold methanol (200 ml.), and ether (750 ml.), to remove an ether-soluble brown impurity. The residual crude *5-benzyloxy-3-formylindole*, m. p. 234—235° (94 g., 85%), crystallised from 4 : 1 dimethylformamide–water (500 ml.) as pale buff prismatic needles, m. p. 239—241° (83 g., 75%). An analytical sample, crystallised from pure dimethylformamide, had m. p. 241—242° (Found: C, 76·6; H, 5·7; N, 5·9. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%). The 2 : 4-dinitrophenylhydrazone had m. p. 278—279°.

5-Benzyloxy-3-2′-nitropropenylindole.—A solution of 5-benzyloxy-3-formylindole (65 g., 0·26 mole) in nitroethane (1920 ml.), containing benzylamine (5·52 g., 0·05 mole), was refluxed for 1 hr. The glistening red plates, m. p. 192—194° (51 g.), which separated on cooling, were filtered off and washed with ether. Recrystallisation from ethanol (3·2 l.) gave pure *5-benzyloxy-3-2′-nitropropenylindole* as prismatic red needles, m. p. 194—196° (47 g., 59%) (Found: C, 69·9; H, 5·5; N, 9·0. $C_{18}H_{16}O_3N_2$ requires C, 70·1; H, 5·2; N, 9·1%). A second crop (2·2 g.) had m. p. 193—195°. Evaporation of the mixture left a tar which was boiled with ethanol (1 l.) and charcoal and filtered. Further product was obtained on cooling as red needles, m. p. 192—195° (15 g.). The total yield of material suitable for the next stage was 64·2 g., 81%.

3-2′-Aminopropyl-5-benzyloxyindole.—A solution of 5-benzyloxy-3-2′-nitropropenylindole (7·7 g., 0·025 mole) in pure dry tetrahydrofuran (90 ml.) was added with stirring to a suspension of lithium aluminium hydride (3·0 g., 0·075 mole) in boiling tetrahydrofuran (100 ml.) at a rate sufficient to maintain reflux. The mixture was refluxed overnight, then cooled, and the excess of hydride decomposed by addition of wet ether (50 ml.) and then water (5 ml.). The complex was decomposed by stirring with 50% aqueous sodium hydroxide (25 ml.). The mixture was filtered through " Hyflo Supercel," and the filter-cake washed with ether (4 × 25 ml.). The organic layer (A) in the filtrate was separated, washed with water (3 × 50 ml.), and extracted with 2N-acetic acid (2 × 50 ml.). The acid solution was made alkaline with 2N-sodium hydroxide and extracted with ether (100; 50; 25 ml.). The ether extracts were washed with water (5 × 30 ml.), dried (Na_2SO_4), and evaporated under reduced pressure, leaving a straw-coloured oily base. This was triturated with N-sulphuric acid, and the crude hygroscopic salt filtered off. After being washed with acetone, 3-2′-aminopropyl-5-benzyloxyindole sulphate had m. p. (e.c.) 139—142° (decomp.) (4·4 g.). Crystallisation from methanol (50 ml.)–ether (450 ml.) raised the m. p. (e.c.) to 146—148° (decomp.) (3·5 g., 41%). A sample of the sulphate

[17] Burton and Leong, *Chem. and Ind.*, 1953, 1035.
[18] Burton and Stoves, *J.*, 1937, 1726.

recrystallised from the same solvents and equilibrated in air formed a *monohydrate* (Found: C, 62·0; H, 6·9; N, 7·8; H_2O, 5·2. $C_{16}H_{20}ON_2,\frac{1}{2}H_2SO_4,H_2O$ requires C, 62·2; H, 6·7; N, 8·1; H_2O, 5·2%). Another sample recrystallised from acetone–water (1 : 2) formed a *dihydrate* on equilibration. This had m. p. (e.c.) 128—131° (decomp.) (Found: C, 59·3; H, 7·1; N, 7·6; S, 4·6; H_2O, 9·2. $C_{16}H_{20}ON_2,\frac{1}{2}H_2SO_4,2H_2O$ requires C, 59·2; H, 6·9; N, 7·7; S, 4·4; H_2O, 9·9%).

A sample of the neutral material left in the organic layer (A) was distilled at 115—120°/0·03 mm. The distillate partly solidified. Recrystallisation from chloroform–light petroleum (b. p. 60—80°) gave straw-coloured needles of *5-benzyloxy-3-hydroxymethylindole*, m. p. 110—112° (Found: C, 75·8; H, 6·35; N, 5·6. $C_{16}H_{15}O_2N$ requires C, 75·9; H, 5·9; N, 5·5%).

3-2′-Aminopropyl-5-hydroxyindole.—Palladium chloride (0·2 g.) and acid-washed charcoal (1·0 g.) were suspended in water (60 ml.) and hydrogenated at room temperature and 1 atm. A suspension of 3-2′-aminopropyl-5-benzyloxyindole sulphate (3·5 g.) in ethanol (90 ml.) was added and the hydrogenation continued under similar conditions. A hydrogen uptake slightly in excess of theory was obtained. The suspension was filtered and the filtrate evaporated, under reduced pressure of hydrogen, leaving 3-2′-aminopropyl-5-hydroxyindole sulphate as a hygroscopic, straw-coloured syrup. After several days' drying over silica gel *in vacuo* at room temperature the syrup (2·5 g.) solidified to form flakes of the *monohydrate*, m. p. (e.c.) 130—133° (decomp.) (Found: C, 51·7; H, 6·8; N, 10·9. $C_{11}H_{14}ON_2,\frac{1}{2}H_2SO_4,H_2O$ requires C, 51·4; H, 6·6; N, 10·9%). Attempts to prepare a creatinine sulphate complex resulted in products containing varying proportions of creatinine sulphate. The picrate had m. p. 218—220° (decomp.).

5-Benzyloxy-3-2′-nitrobutenylindole.—A solution of 5-benzyloxy-3-formylindole (42 g.) in 1-nitropropane (1260 ml.) containing benzylamine (4·2 g.) was refluxed for 42 hr. The solution was concentrated by half under reduced pressure and set aside at 0°. The crystalline *product* (23 g.), m. p. 172—173°, was filtered off, washed with ether, combined with a second crop (7 g.; m. p. 171—172°), resulting from further concentration of the nitropropane, and recrystallised from ethanol (935 ml.). The prismatic red needles (23·1 g.) had m. p. 173—174° (Found: C, 70·8; H, 5·8; N, 8·7. $C_{19}H_{18}O_3N_2$ requires C, 70·8; H, 5·6; N, 8·7%). Further product was obtained by evaporating the reaction liquors to a syrup and after one recrystallisation was suitable for the next stage (7·4 g., m. p. 170—173°). The total yield of recrystallised material was 57%.

3-2′-Aminobutyl-5-benzyloxyindole.—A solution of 5-benzyloxy-3-2′-nitrobutenylindole (17·5 g.) in dry tetrahydrofuran (190 ml.) was reduced with lithium aluminium hydride as described for the nitropropenyl compound, except that the reaction time was reduced to 45 min. after completion of the addition. The resultant base was triturated with N-sulphuric acid, and the off-white hygroscopic sulphate (8·8 g.) washed with acetone. After crystallisation from ethanol, the m. p. (e.c.) was 185—187° (8·1 g., 41%). Recrystallisation from methanol (140 ml.)–ether (220 ml.) gave the pure *monohydrate*, m. p. (e.c.) 189—190° (Found: C, 62·8; H, 7·1; N, 7·5; S, 4·5. $C_{16}H_{22}ON_2,\frac{1}{2}H_2SO_4,H_2O$ requires C, 63·1; H, 6·7; N, 7·8; S, 4·4%).

Neutral material, isolated as in the reduction of the nitropropenyl compound, had m. p. 109—110°, undepressed on admixture with 5-benzyloxy-3-hydroxymethylindole.

3-2′-Aminobutyl-5-benzyloxyindole (from 5-Benzyloxygramine).—5-Benzyloxygramine [8] (20 g.) was dissolved in 1-nitropropane (90 ml.) under nitrogen. The solution was stirred and refluxed for 5 hr. during which at least 70% of the theoretical quantity of dimethylamine was evolved. The cooled mixture was acidified with 10% aqueous acetic acid and extracted with ether (400 ml.). The extract was washed with water (5 × 100 ml.), dried (Na_2SO_4), and evaporated, leaving crude 5-benzyloxy-3-2′-nitrobutylindole as an orange-red oil (19·8 g.).

Part (16 g.) of the foregoing crude oil was hydrogenated in ethanol at 70° and 400 lb./sq. in. with a Raney nickel catalyst. After 100% hydrogen uptake the filtered solution was evaporated under reduced pressure, leaving an oil which was taken up in ether (150 ml.) and extracted with 2N-acetic acid (75; 50; 2 × 20 ml.). The acid extract was washed with ether (2 × 50 ml.) and basified to pH 10 with 2N-sodium hydroxide. The alkaline suspension was extracted with ether (100; 3 × 35 ml.) and the dried (Na_2SO_4) ether solution evaporated, leaving a sticky solid (9·5 g.). Trituration with an equivalent of 2N-sulphuric acid, and crystallisation from aqueous ethanol, gave 3-2′-aminobutyl-5-benzyloxyindole sulphate hydrate, m. p. (e.c.) 185—188° (8·5 g., 40% from 5-benzyloxygramine). Recrystallisation from methanol–ether gave the pure sulphate, m. p. (e.c.) 190—191°. This compound, although forming a *hydrate*

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containing 1·6 H_2O, did not depress the m. p. of the sample prepared from 5-benzyloxy-3-2′-nitrobutenylindole (see above) and had an identical infrared spectrum (Found: C, 61·3; H, 7·8; N, 7·6; S, 4·7. $C_{18}H_{22}ON_2,\frac{1}{2}H_2SO_4,1{\cdot}6H_2O$ requires C, 61·5; H, 7·1; N, 7·6; S, 4·3%).

3-2′-Aminobutyl-5-hydroxyindole.—3-2′-Aminobutyl-5-benzyloxyindole sulphate (3·4 g.) in ethanol (115 ml.) was hydrogenated in the presence of palladium as described for the aminopropyl compound. Drying the product over silica gel *in vacuo* at room temperature gave flakes of *3-2′-aminobutyl-5-hydroxyindole sulphate monohydrate* (2·4 g.), m. p. (e.c.) 148—150°, 155° (decomp.) (Found: C, 53·1; H, 6·9; N, 10·3; S, 5·9. $C_{12}H_{16}ON_2,\frac{1}{2}H_2SO_4,H_2O$ requires C, 53·1; H, 7·1; N, 10·3; S, 5·9%). Treatment with ethanolic picric acid gave a *dipicrate*, m. p. 176—177° (Found: C, 43·8; H, 3·8; N, 16·5. $C_{12}H_{16}ON_2,2C_6H_3O_7N_3$ requires C, 43·5; H, 3·4; N, 16·9%).

5-Benzyloxy-3-2′-nitrovinylindole.—A suspension of 5-benzyloxy-3-formylindole (25 g.) in nitromethane (990 ml.) containing benzylamine (2·5 g.) was heated under reflux for 4 hr. The dark red solution was evaporated to ¼ volume under reduced pressure of nitrogen. On storage at 0°, *5-benzyloxy-3-2′-nitrovinylindole* separated (m. p. 176—177°; 17·6 g., 60%). Recrystallisation from ethanol (900 ml.) gave red hexagonal plates, m. p. 179—180° (13·6 g.) (Found: C, 69·6; H, 5·2; N, 9·0. $C_{17}H_{14}O_3N_2$ requires C, 69·4; H, 4·8; N, 9·5%).

3-2′-Aminoethyl-5-benzyloxyindole.—A solution of 5-benzyloxy-3-2′-nitrovinylindole (7·3 g.) in dry tetrahydrofuran (90 ml.) was reduced with lithium aluminium hydride as described for the nitropropenyl compound except that the reaction time after addition was only an ½ hr. The straw-coloured oily base (4·4 g.) was triturated with N-sulphuric acid, and the sulphate, m. p. (e.c.) 230—232°, sintering at 178—181° (4·1 g., 51%), was filtered off and washed with ice-cold acetone. Recrystallisation from ethanol and equilibration in air gave the pure sulphate monohydrate, m. p. (e.c.) 230—232°, sintering at 187—189° (Found: C, 61·1; H, 6·1; N, 8·5; S, 5·1. Calc. for $C_{17}H_{18}ON_2,\frac{1}{2}H_2SO_4,H_2O$: C, 61·3; H, 6·3; N, 8·4; S, 4·8%).

3-2′-Aminoethyl-5-hydroxyindole (*Serotonin*).—5-Benzyloxy-3-2′-aminoethylindole sulphate monohydrate (10·0 g., 0·03 mole) in ethanol (180 ml.) was hydrogenated in the presence of palladium as described for the aminopropyl compound. The crude 5-hydroxytryptamine sulphate was dissolved in a solution of creatinine sulphate hemihydrate (5·13 g., 0·03 mole) in water (35 ml.), and hot acetone (200 ml.) was added. After storage at 0°, the resultant 5-hydroxytryptamine creatinine sulphate monohydrate, m. p. (e.c.) 217—219° (decomp.) (11·5 g., 94%), was filtered off and washed with acetone. Two recrystallisations, by dissolution in hot water (96 ml.), addition of charcoal, filtration, and addition of ethanol (64 ml.) to the filtrate, gave almost colourless prisms, m. p. (e.c.) 219—221° (decomp.) (7·5 g., 67%) (Found: C, 41·5; H, 5·7; S, 8·1; H_2O, 4·6. Calc. for $C_{14}H_{19}O_2N_5,H_2SO_4,H_2O$: C, 41·5; H, 5·7; S, 7·9; H_2O, 4·5%). Speeter and his collaborators [19] give m. p. (Kofler) 214—216°.

3-2′-Nitropropenylindole.—3-Formylindole (2·5 g.), suspended in nitroethane (15 ml.) containing benzylamine (0·19 g.), was refluxed for 1 hr. The orange-red solid which separated on cooling recrystallised from methanol (70 ml.), giving *3-2′-nitropropenylindole* as orange plates, m. p. 193—195° (1·8 g., 51%) (Found: N, 13·9. $C_{11}H_{10}O_2N_2$ requires N, 13·9%).

3-2′-Aminopropylindole.—A solution of 3-2′-nitropropenylindole (2·2 g.) in dry tetrahydrofuran was reduced with lithium aluminium hydride as described for the corresponding 5-benzyloxy-compound. Distillation of the waxy base at 125—130°/0·04 mm. gave 3-2′-aminopropylindole as a colourless solid, m. p. 94—96° (0·6 g.). Redistillation raised the m. p. to 97—98° (shrinkage at 96°) (Found: C, 76·1; H, 8·4; N, 16·2. Calc. for $C_{11}H_{14}N_2$: C, 75·8; H, 8·1; N, 16·1%).

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[19] Speeter, Heinzelmann, and Weisblatt, *J. Amer. Chem. Soc.*, 1951, **73**, 5514.

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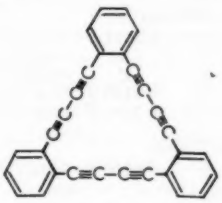
791. *Calculated Bond Lengths in Some Cyclic Compounds. Part V.** 1 : 2-7 : 8-13 : 14-*Tribenzocyclooctadeca*-1 : 7 : 13-*triene*-3 : 5 : 9 : 11 : 15 : 17-*hexayne and Diphenyldiacetylene.*

By T. H. Goodwin.

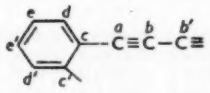
Energy levels, bond orders, and bond lengths in these compounds have been derived by the molecular-orbital technique, corrections being applied, by successive approximations, to the exchange integrals H_{rs} for their dependence on bond length.

The results for diphenyldiacetylene suggest that a further study of bond orders and lengths in conjugated acetylenes is called for.

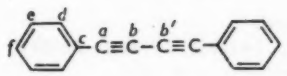
The preparation of a yellow highly crystalline substance tentatively described as the novel macrocycle 1 : 2-7 : 8-13 : 14-tribenzo*cyclo*octadeca-1 : 7 : 13-triene-3 : 5 : 9 : 11 : 15 : 17-hexayne (I) has been recorded recently by Eglinton and Galbraith [1] although, owing to its instability, final establishment or denial of the postulated structure is proving difficult.[2] *X*-Ray examination is being carried out in this department by Dr. J. C. Speakman and Mr. W. K. Grant, and a calculation of the expected bond lengths in (I), subsequently referred to as " the triangle," is of great interest in anticipation of their results. Especially interesting are the lengths of the formal single bonds in the butadiyne arms of the triangle



(I)



(II)



(III)

because a number of similarly situated single bonds have been found to be remarkably short. For example, the central link in diacetylenedicarboxylic acid dihydrate measures [3] 1·33 ± 0·02 Å, and so is even shorter than the double bond in ethylene found by Pauling and Brockway [4] to be 1·34 ± 0·02 and by Galloway and Barker [5] to be 1·353 ± 0·01 Å. In the same way the middle bond in diacetylene itself is reported [6] as 1·36 ± 0·03 Å.

Bond lengths have now been calculated for " the triangle " by the molecular-orbital technique, group theoretical methods being used to simplify the calculations. These fall into three parts because the p_z-electrons on the carbon atoms of the butadiyne chains interact with each other and with the p_z-electrons on the carbon atoms of the benzene rings and so form a π-molecular orbital system spreading over all thirty carbon atoms of " the triangle." The p_y-electrons of the atoms in the butadiyne chains are, on the other hand, confined to these chains since the remaining valency-shell orbitals of the benzenoid carbon atoms are engaged in sp^2-hybridisation and the formation of σ-bonds and so cannot react appreciably with them. Thus the p_y- and p_z-atomic orbitals, giving rise to π_y- and π_z-molecular orbitals, must be handled separately and then combined to derive the interatomic distances.

π_z-Molecular Orbitals.—The molecule has D_{3h} symmetry and consideration of the

* Part IV, *J.*, 1956, 3595.

[1] Eglinton and Galbraith, *Proc. Chem. Soc.*, 1957, 350.
[2] Dr. A. Eglinton, personal communication.
[3] Dunitz and Robertson, *J.*, 1947, 1145.
[4] Pauling and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 1223.
[5] Galloway and Barker, *J. Chem. Phys.*, 1942, **10**, 88.
[6] Pauling, Springall, and Palmer, *J. Amer. Chem. Soc.*, 1939, **61**, 927.

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character table [7] shows that the π_z-molecular orbital energy levels must be $10E'' + 5A_1'' + 5A_2''$, the E'' levels being doubly degenerate. Thus the thirtieth-order secular determinant breaks down into two (identical) tenth- and two (different) fifth-order ones.

To avoid begging the question we must begin by assuming that all exchange integrals H_{rs} between orbitals on neighbouring atoms r, s are equal. This is done in spite of the fact that one expects H_{H-C} and $H_{H\equiv C}$ to be respectively smaller and larger than $H_{ar-ar} = \beta$, the integral between neighbouring orbitals on carbon atoms (taken as 1·39 Å apart) in benzene, since the interatomic distances are in the order pure single bond > benzene bond > pure triple bond. All other exchange integrals and all overlap integrals are assumed to be zero.

With these approximations the energy levels $E - \alpha$ (α being the Coulomb integral for carbon) for this first iteration were obtained (Table 1) by well-established methods, and hence the total π_z-bond orders p_z were calculated.* These are given in Table 2 for the seven distinctly different bonds of the molecule which, for greater convenience of reference, are indicated as in (II), the repeat pattern of the molecule.

TABLE 1. *Energy levels of π-orbitals in "the triangle." (Only occupied levels are given and these are numbered within each symmetry class in order of increasing energy in the third iteration.)*

Symmetry class	Orbital number	$E - \alpha$ 1st Iteration	2nd Iteration	3rd Iteration	Symmetry class	Orbital number	$E - \alpha$ 1st Iteration	2nd Iteration	3rd Iteration
	(i) π_z-Orbitals					(i) π_z-Orbitals			
A_2''	1	2·3028 β	2·4089 β	2·3529 β	E''	3	1·3591 β	1·4142 β	1·4444 β
E''	1	2·2504 β	2·3184 β	2·2593 β	E''	4	β	0·9990 β	1·0036 β
E''	2	1·7321 β	2·0063 β	2·0152 β	A_2''	3	β	0·9234 β	0·9489 β
A_2''	2	1·6180 β	1·8288 β	1·8425 β	A_1''	2	0·6180 β	0·8476 β	0·9057 β
A_1''	1	1·3028 β	1·4235 β	1·4587 β	E''	5	0·3287 β	0·5890 β	0·7214 β
	(ii) π_y-Orbitals					(ii) π_y-Orbitals			
A_u	1	1·6180 β	2·1747 β	2·0964 β	B_g	1	0·6180 β	1·1047 β	1·2364 β

TABLE 2. *Exchange integrals (β_{rs}), partial (p_z and p_y) and total (p) mobile bond orders, and lengths (L) in "the triangle."*

Bond	Iteration	β_{rs}	p_z	p_y	p	L	Bond	Iteration	β_{rs}	p_z	p_y	p	L
ab	1	1	0·7463	0·8943	1·6406	1·230	*cd*	1	1	0·5905		0·5905	1·410
	2	1·55	0·8895	0·9453	1·8348	1·214		2	0·93	0·6279		0·6279	1·397
	3	1·61	0·9296	0·9661	1·8957	1·209		3	0·97	0·6370		0·6370	1·394
ac	1	1	0·4887		0·4887	1·449	*de*	1	1	0·6898		0·6898	1·380
	2	0·80	0·3160		0·3160	1·485		2	1·03	0·6905		0·6905	1·380
	3	0·71	0·2590		0·2590	1·489		3	1·03	0·6855		0·6855	1·381
bb'	1	1	0·5436	0·4473	0·9909	1·369	*ee'*	1	1	0·6286		0·6286	1·396
	2	1·07	0·3390	0·3263	0·6652	1·432		2	0·97	0·6312		0·6312	1·395
	3	0·86	0·2763	0·2580	0·5343	1·441		3	0·98	0·6407		0·6407	1·393
cc'	1	1	0·5197		0·5197	1·436							
	2	0·85	0·6024		0·6024	1·406							
	3	0·94	0·6290		0·6290	1·396							

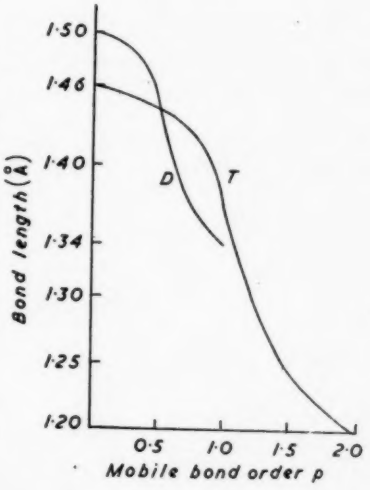
π_y-Molecular Orbitals.—The three sets of p_y-atomic orbitals of the butadiyne chains must, with the many other atomic orbitals which are symmetrical about the plane of the nuclei, conform collectively to the D_{3h} symmetry of the whole molecule. However, the non-interaction of these two groups of orbitals makes it very much easier to consider the butadiyne sets separately from the start than to factorise them out later, so this has been done. In this first iteration, there are, therefore, three sets of π_y-molecular orbitals which

* It is customary to use p (with or without subscript) as symbol for atomic orbitals of quantum number $l = 1$ as well as for bond orders, but care has been taken to make clear which is implied in each case.

[7] Herzberg, "Infra-red and Raman Spectra," van Nostrand Co., New York, 1945, p. 117.

are identical with the π-orbitals of butadiene as calculated with equal exchange integrals between neighbouring atomic orbitals. Their energies are included in Table 1 and the corresponding total π_y-bond orders p_y in Table 2.

Total Bond Orders and Derived Bond Lengths.—The total mobile bond orders for all electrons are given as $p = p_y + p_z$. To convert these into bond lengths two correlation curves have been used. The first was established in Fig. 1 of Part I [8] and is shown as curve *D* in the Figure of the present paper. This has been used for all C–C bonds except *ab* and *bb'*. For these a new curve has been derived as follows. In a system such as " the triangle " the π_y- and π_z-orbitals cannot interact but do intersect in the line of the butadiyne carbon nuclei. Hence what are essentially two butadiene systems are superposed in each of these regions and so the correlation curve should be, not one based on the extrapolation of curve *D* to a point appropriate to acetylene ($p = 2$, $L = 1{\cdot}20$ Å), but one, *T*, obtained by doubling the mobile order scale ($0 < p < 2$) and extending and displacing the length scale to cover the range $1{\cdot}46 > L > 1{\cdot}20$ Å. The graph then passes through the points (0, 1·46), (0·2, 1·455), (0·4, 1·447), (0·6, 1·437), (0·8, 1·420), (1·0, 1·367), (1·2, 1·307), (1·4, 1·262), (1·6, 1·234), (1·8, 1·216), (2·0, 1·20). The value 1·46 Å for the pure single bond ($p = 0$) formed by *sp*-hybridised orbitals results from the argument that, just as the pure single bond formed by sp^3-hybrids is shortened [9] by 0·04 Å when the hybridisation becomes sp^2, so a similar further shortening is to be expected on passing to *sp*-hybridisation. A comment is made later on the value 1·20 Å for C≡C in a pure triple bond.



It might be objected that this is a rather arbitrary technique for converting bond orders into bond lengths since it implies that, however *p* is made up from p_y and p_z, the same bond length is obtained. This is so, but the same criticism is applicable to the combination of the partial (one-electron) bond orders which make up p_y and p_z and could only be overcome by applying a self-consistent field technique. In any case it would be impracticable to derive bond lengths L_y and L_z from p_y and p_z and then combine them to obtain substantially shorter lengths *L* for the complete multiple bond.

From curve *T*, then, are obtained lengths *L* for the bonds *ab* and *bb'*, while curve *D* is used for all other C–C bonds. These lengths are given in Table 2 and suggest that the formal single bonds *ac* and *bb'* are much shorter than might have been expected (1·50 and 1·46 Å, respectively), the triple bond *ab* rather longer (1·20 Å) than, and the benzene ring bonds not much different from expectation (1·39 Å) apart from *cc'* which seems surprisingly large and distorts the hexagon appreciably. However, these deviations are all attributable to the naïve assumption that all H_{rs} between neighbour orbitals are equal to β. To try to correct for this the bond lengths *L* obtained in the first iteration were used to give improved integrals H_{rs} by means of the table given by Mulliken, Rieke, and Brown.[10] These are recorded in Table 2 as multiples of β.

Second and Third Iterations.—Energy levels, bond orders and lengths for the second iteration were obtained as before (Tables 1 and 2). The new bond lengths are more realistic. The links comprising the benzene rings are now approximately equal though

[8] Goodwin and Vand, *J.*, 1955, **1683**.
[9] Coulson, Victor Henri Memorial Volume, Contribution a l'Étude de la Structure Moléculaire Desoer, Liège, 1948, p. 15.
[10] Mulliken, Rieke, and Brown, *J. Amer. Chem. Soc.*, 1941, **63**, 48.

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cc' is still slightly longer than the rest. The formal triple bonds are of about the expected length though the " diacetylene single bond " *bb'* is much longer than originally, having now a mobile order of only 0·665 from both π_y- and π_z-orbitals. Increasing H_{a5} must, of course, decrease the order and increase the length of both *ac* and *bb'* but it is perhaps surprising that the former has gone up to 1·485 Å in length. In fact, the results as a whole should warn against confidence in calculations in which all exchange integrals are equalised in spite of differences in bond type.

Since the second iteration made so great a difference to the estimated bond lengths, a third cycle of operations was carried out to give the further energies, orders, and lengths recorded in Tables 1 and 2, the H_{rs} values being obtained from the lengths given by the second cycle.

The interatomic distances obtained in this iteration differed so little from those obtained in the second that they were supposed now to have converged to the ultimate values appropriate to this type of calculation. Although they are given to a third decimal place, it is not suggested that they are reliable beyond the second; the third is given to facilitate their use in later work.

When this type of calculation is carried out on aromatic condensed-ring hydrocarbons the derived bond lengths agree with good *X*-ray measurements to within ±0·02 Å. There are fewer acetylenic compounds on which *X*-ray measurements and molecular-orbital calculations have been made, but it seems likely that the present bond lengths in the benzene rings should be within ±0·02 Å of the experimental values when available, and the remaining inter-carbon bonds within about ±0·04 Å. However, to permit comparison with a closely similar compound on which experimental measurements have been made, calculations corresponding to the foregoing have now been made on diphenyldiacetylene and are described later. Anticipating these results, we may say that the above conclusions about the reliability of the calculations on " the triangle " seem justified.

Ultraviolet Absorption Spectrum.—The ultraviolet spectrum [1] of the yellow compound shows rather more than twenty peaks, many of which must represent vibrational structure. Although this spectrum cannot be adduced as conclusive confirmation of the structure (I), yet it is consistent with it, as can be seen by correlating it with the calculated transition energies. Above 250 mμ there appear to be three separate electronic transitions with their origins near 23,000 ($\varepsilon_{max.}$ 1600), 27,800 ($\varepsilon_{max.}$ 10,500), and 33,170 ($\varepsilon_{max.}$ 234,400) cm.$^{-1}$. From simple considerations these should involve the promotion of one electron from one of the highest occupied degenerate pair ($5e''$) of orbitals to one of the lowest unoccupied degenerate pair ($6e''$). This promotion gives rise to three excited electronic states $E'' \times E'' = A_1' + A_2' + E'$. Transitions from the ground state A_1' to the states A_1' and A_2' are forbidden in absorption, while the transition to the state E' is allowed and should occur with high intensity. On this basis, the intense band at 33,170 cm.$^{-1}$ would mark the allowed transition $A_1' \longrightarrow E'$ which is polarised in the plane of the molecule. The bands at lower frequency may represent the forbidden transitions $A_1' \longrightarrow A_1'$ and $A_1' \longrightarrow A_2'$ intensified by transfer from the allowed transition. Whether the 27,800 cm.$^{-1}$ transition belongs to $A_1' \longrightarrow A_2'$ and the 23,300 cm.$^{-1}$ transition to $A_1' \longrightarrow A_1'$ or *vice versa* is a matter for further calculations, but it is noteworthy that the calculated transition energy of $2 \times 0{\cdot}72\beta$ corresponds to *ca.* 28,800 cm.$^{-1}$ (if $\beta \approx 20{,}000$ cm.$^{-1}$), which is almost exactly the *average* energy of the three transitions (28,100 cm.$^{-1}$); if, however, allowance of 5000 cm.$^{-1}$ is to be made [11] for singlet–triplet splitting, β would have to be 16,000 cm.$^{-1}$. This, though rather low, is still of the correct order of magnitude. Further, the intensity of the putative forbidden transitions can be explained by using a matrix element for intensity transfer of about the same size as that deduced from the spectrum of benzene.

Diphenyldiacetylene.—Partly to check the remarkable change in length of the bond

[11] Platt, *J. Chem. Phys.*, 1951, **19**, 1418.

bb' of " the triangle " between the first and the second iteration, and partly to provide an estimate of the likely deviation between observed and calculated lengths, the interatomic distances in diphenyldiacetylene (III) were calculated for comparison with Wiebenga's measurements.[12] The π-orbital energies are shown in Table 3 for each of the three iterations, and the exchange integrals, bond orders, and bond lengths are given in Table 4, all being determined by the methods described for " the triangle." Table 4 also includes Wiebenga's measurements (all of which he claims to be accurate to ±0·03 Å) and the discrepancy $\Delta = L_{obs.} - L_{calc.}$ At all stages the computations on both (I) and (III) ran closely parallel, thereby confirming both the arithmetic and the technique of successive approximations.

TABLE 3. *Energy levels of π-orbitals in diphenyldiacetylene. (Only occupied levels are given, and these are numbered within each symmetry class in order of increasing energy in the third iteration.)*

		$E - \alpha$					$E - \alpha$	
Symmetry	Orbital number	1st Iteration	2nd Iteration	3rd Iteration	Symmetry	Orbital number	1st Iteration	2nd Iteration	3rd Iteration
	(i) π_y-Orbitals					(i) π_y-Orbitals			
B_{3u}	1	2·1829 β	2·3297 β	2·2899 β	B_{1g}	1	β	1·0200 β	β
B_{2g}	1	2·1227 β	2·0516 β	2·0834 β	A_u	1	β	1·0200 β	β
B_{3u}	2	1·6673 β	1·9018 β	1·9029 β	B_{2u}	3	β	0·9511 β	0·9913 β
B_{2g}	2	1·3417 β	1·4104 β	1·4412 β	B_{2g}	3	0·3859 β	0·6905 β	0·7995 β
	(ii) π_z-Orbitals					(ii) π_z-Orbitals			
B_{2u}	1	1·6180 β	2·1578 β	2·0964 β	B_{2g}	1	0·6180 β	1·1278 β	1·2364 β

TABLE 4. *Exchange integrals, partial and total mobile bond orders, and lengths in diphenyldiacetylene.*

Bond	Iteration	β_{rs}	p_z	p_y	p	L	$L_{obs.}$	Δ
ab	1	1	0·7814	0·8943	1·6757	1·227		
	2	1·56	0·9042	0·9496	1·8538	1·214		
	3	1·61	0·9331	0·9661	1·8992	1·209	1·18	−0·03
ac	1	1	0·4442		0·4442	1·467		
	2	0·76	0·2871		0·2871	1·487		
	3	0·70	0·2470		0·2470	1·490	1·44	−0·05
bb'	1	1	0·5127	0·4473	0·9600	1·381		
	2	1·03	0·3384	0·3134	0·6518	1·433		
	3	0·86	0·2740	0·2580	0·5320	1·441	1·39	−0·05
cd	1	1	0·5962		0·5962	1·408		
	2	0·93	0·6337		0·6337	1·395		
	3	0·98 *	0·6456		0·6456	1·391		
de	1	1	0·6827		0·6827	1·383		
	2	1·02	0·6807		0·6807	1·382		
	3	1·02 *	0·6709		0·6709	1·385		
fe	1	1	0·6552		0·6552	1·390		
	2	1·00	0·6585		0·6585	1·388		
	3	1·00	0·6640		0·6640	1·387		

* Assumed = 1·00 although derived as stated.

Agreement between observed and calculated interatomic distances is, not surprisingly, excellent in the benzene rings.

The discrepancy Δ_{ab} for the acetylenic links is well within the limit admitted both experimentally and theoretically. Its negative sign is probably due either to the selection of acetylene as the standard triple bond or to the use of *X*-ray crystallography for the measurement of diphenyldiacetylene, for there is a marked tendency (Table 5) for spectroscopic methods to give interatomic distances of about 1·20 Å in C≡C while *X*-ray investigations lead to slightly shorter lengths though dimethyltriacetylene is exceptional in this respect. It is usual to suggest that the inter-carbon distance in acetylene may be slightly

[12] Wiebenga, *Z. Krist.*, 1940, **102**, 193.

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too great for a pure triple bond by reason of the small negative charges which incipient ionisation of the hydrogen atoms would confer on the carbons. A similar repulsion between negatively charged carbon atoms might apply to symmetrical dihalogenoacetylenes as a result of the high electronegativity of the halogen atoms. Again, in the symmetrical compounds studied by *X*-rays, the central bonds whether triple or single will be slightly elongated as a result of the net changes which any hetero-atoms in the system will induce, though these elongations may well be too small to take into account in any theoretical estimate of bond length. However, multiple bonds in conjugated systems must be longer than in isolation other things being equal, and so the *X*-ray results suggest that curve *T* should perhaps have been drawn to a point $p = 2, L = 1{\cdot}17$ Å (say); it is unfortunate that the central bond of di-*tert.*-butylacetylene has never been measured. Further, while spectroscopic measurements lead to internuclear distances, *X*-ray studies give distances between centres of electron density; these are not necessarily the same, and correlation curves between order and length should relate to one experimental method only. Work is therefore planned to investigate this matter further. Meanwhile, for want of a better, curve *T* must be used.

TABLE 5. *Lengths of some* C≡C *bonds.*

[M.W. = Microwave; Sp = spectroscopic measurements; E.D. = electron diffraction; E.D.S. = electron diffraction sector technique; X.R. = *X*-ray measurements on crystals.]

Compound	Length (Å)	Method	Ref.
Chloroacetylene	1·211 ± 0·001	M.W.	14
Acetylene	1·207 ± 0·002	Sp.	13
Methylacetylene	1·2073	M.W.	15
,,	1·207 ± 0·002	M.W.	16
Cyanoacetylene	1·203	M.W.	17
Methylcyanoacetylene	1·203	M.W.	18
Dibromoacetylene	1·20 ± 0·03	E.D.	19
Dimethyldiacetylene	1·20 ± 0·02	E.D.	5
Dimethyltriacetylene	1·199 ± 0·01	X.R.	20
Dichloroacetylene	1·195	E.D.S.	21
Diacetylene	1·19 ± 0·03	E.D.	5
Acetylenedicarboxylic acid dihydrate	1·19 ± 0·02	X.R.	22
Tolan	1·19 ± 0·02	X.R.	23
Diacetylenedicarboxylic acid dihydrate	1·185 ± 0·02	X.R.	2
Diphenyldiacetylene	1·18 ± 0·03	X.R.	12
Di-iodoacetylene	1·18	E.D.	19

The formal single bonds *ac* and *bb'* as determined in the first iteration are respectively 0·03 Å longer and 0·01 Å shorter than observed. These deviations are within the experimental error indicated by Wiebenga, but it is impossible to believe that all exchange integrals between neighbouring atomic orbitals are the same, and so this agreement between observed and calculated interatomic distances must be ignored. In the third iteration, $\Delta = -0{\cdot}05$ Å for each of these links and this seems rather large. The calculations may be at fault in the correlation of bond length with either (*a*) exchange integral, though from the method of derivation [10] this does not seem likely to be serious, or (*b*) bond order. There have been very few correlations of bond order and bond length in acetylenes

[13] Herzberg, *op. cit.*, p. 398.
[14] Westenberg, Goldstein, and Wilson, *J. Chem. Phys.*, 1949, **17**, 1319.
[15] Thomas, Sherrard, and Sheridan, *Trans. Faraday Soc.*, 1955, **51**, 623.
[16] Trambarulo and Gordy, *J. Chem. Phys.*, 1950, **18**, 1613.
[17] Westenberg and Wilson, *J. Amer. Chem. Soc.*, 1950, **72**, 199.
[18] Sheridan and Thomas, *Nature*, 1954, **174**, 798.
[19] Brockway, *Rev. Mod. Phys.*, 1936, **8**, 231.
[20] Jeffrey and Rollett, *Proc. Roy. Soc.*, 1952, *A*, **213**, 86.
[21] Finbak and Hassel, *Arch. Math. Naturv.*, 1941, **44**, No. 3; Hassel and Taarland, *Tidsskr. Kjemi Bergvesen Met.*, 1941, **1**, 172.
[22] Dunitz and Robertson, *J.*, 1947, 148.
[23] Robertson and Woodward, *Proc. Roy. Soc.*, 1938, *A*, **164**, 436.

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which have taken account of the variation of H_{rs} with interatomic distance and further investigations of this are proposed. There is, of course, the third possibility that the *X*-ray measurements, carried out nearly twenty years ago, are rather less accurate than was supposed.

Dr. G. Eglinton is thanked for helpful discussion, and Dr. J. C. D. Brand for helpful discussions and for his correlation of the ultraviolet absorption spectrum of the yellow substance with the molecular-orbital energy levels of " the triangle."

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792. *Adsorption on Oxide Gels from Binary Liquid Mixtures: Some Activity Coefficients of Materials at Surfaces.*

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Activity coefficients are presented for adsorption at surfaces from binary liquid mixtures on alumina, silica, and titania gels respectively. Two of the three types of behaviour observed with carbon adsorbents are again observed with oxide gels. The nature of adsorption is controlled mainly by the polar nature of the adsorbents, the gels being very similar to one another. As compared with carbon adsorbents they show a much greater discrimination between polar and non-polar liquids.

IN the study of adsorption by solids from liquids, the evaluation of surface activity coefficients for the adsorbates provides one way in which the adsorptive characteristics of the solids can be compared irrespective of their specific surface areas. If, moreover, these coefficients are compared with the activity coefficients for the same components in the bulk liquid, a qualitative indication is obtained of the importance of the forces acting between solid and liquid compared with those between liquid and liquid.

Elton [1] discussed pairs of completely miscible liquids. Subsequently, data were presented for adsorption from a range of liquid mixtures on carbon adsorbents.[2] Three types of behaviour were found, as shown by the curves of surface activity coefficient against composition of the surface phase: Type I, in which the curves showed no inflexion; Type II, in which an inflexion was shown; Type III, in which the curves were clearly shown to cross. The relationship between these curves and the other adsorption data (isotherms of concentration change and individual adsorption isotherms) was pointed out.

We now record the corresponding results for adsorption on the more polar surfaces of alumina, silica gel, and titania gel. As previously,[2] $f_1 = a_1/x_1$ and $f_1^s = a_1^s/x_1^s$, where f_1 and f_1^s are the activity coefficients of substance 1 in the liquid and surface phases respectively, a_1 and a_1^s are the corresponding activities, and x_1 and x_1^s are the corresponding mole fractions. The adsorption measurements which lead to values of x_1 and x_2 have been published.[3-5] Values for a_1 and a_2 are obtained from vapour-pressure data; those which have not been published previously are incorporated in the Tables. With the convention used previously, $a_1 = a_1^s$, and values for f_1^s and f_2^s can therefore readily be calculated.

[1] Elton, *J.*, 1954, 3813.
[2] Blackburn, Kipling, and Tester, *J.*, 1957, 2373.
[3] Kipling and Peakall, *J.*, 1956, 4828; 1957, 4054; 1958, 184.
[4] *Idem*, *J.*, 1957, 834.
[5] Allen, Lingo, and Felsing, *J. Phys. Chem.*, 1939, **43**, 425.

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Benzene–cyclohexane–boehmite (Type II)

x_1 (C_6H_6)	x_1^s	f_1^s	f_2^s
0·10	0·457	0·363	1·66
0·20	0·605	0·471	2·05
0·30	0·713	0·555	2·52
0·40	0·795	0·620	3·12
0·50	0·846	0·689	3·65
0·60	0·878	0·763	3·88
0·70	0·902	0·829	3·90
0·80	0·925	0·887	3·72
0·90	0·949	0·950	3·10

Ethylene dichloride–benzene–boehmite (Type I)

x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s
0·10	0·252	0·397	1·20
0·20	0·433	0·462	1·41
0·30	0·578	0·519	1·66
0·40	0·681	0·587	1·88
0·50	0·768	0·651	2·16
0·60	0·832	0·721	2·38
0·70	0·892	0·785	2·78
0·80	0·929	0·861	2·82
0·90	0·968	0·930	3·13

Methyl acetate–benzene–boehmite (Type I)

x_1 (MeOAc)	x_1^s	f_1^s	f_2^s
0·10	0·529	0·268	2·04
0·20	0·665	0·430	2·72
0·30	0·760	0·534	3·67
0·40	0·828	0·612	4·40
0·50	0·878	0·682	5·39
0·60	0·913	0·742	6·33
0·70	0·942	0·805	7·26
0·80	0·966	0·871	8·38
0·90	0·982	0·939	9·94

Chloroform–benzene–boehmite ($p_1^\circ = 159·6$; $p_2^\circ = 74·1$) (Type I)

x_1 ($CHCl_3$)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·10	0·93	1·00	0·271	0·343	1·23
0·20	0·94	1·00	0·488	0·383	1·56
0·30	0·95	1·00	0·642	0·445	1·94
0·40	1·00	0·99	0·749	0·534	2·37
0·50	0·98	0·98	0·822	0·599	2·76
0·60	0·99	0·95	0·878	0·677	3·10
0·70	1·00	0·97	0·923	0·757	3·49
0·80	1·00	0·86	0·957	0·836	3·98
0·90	1·00	0·81	0·984	0·916	4·94

n-*Butyl alcohol–benzene–boehmite (Type II)*

x_1 (Bu^nOH)	f_1	f_2	x_1^s	x_2^s	f_1^s	f_2^s
0·10	3·57	1·06	0·707	0·293	0·505	3·25
0·20	3·11	1·13	0·720	0·280	0·862	3·23
0·30	2·59	1·23	0·730	0·270	1·06	3·19
0·40	2·02	1·35	0·730	0·270	1·11	3·01
0·50	1·71	1·53	0·740	0·260	1·15	2·95
0·60	1·42	1·75	0·750	0·250	1·14	2·80
0·70	1·24	2·02	0·773	0·227	1·13	2·67
0·80	1·12	2·42	0·773	0·227	1·17	2·13
0·90	1·04	2·88	0·804	0·196	1·16	1·47

*Methyl acetate–ethylene dichloride–boehmite * ($p_1^\circ = 168·4$; $p_2^\circ = 61·0$) (Type I)*

x_1 (MeOAc)	x_1^s	f_1^s	f_2^s
0·10	0·543	0·184	1·97
0·20	0·667	0·300	2·40
0·30	0·751	0·400	2·81
0·40	0·816	0·490	3·27
0·50	0·869	0·575	3·82
0·60	0·910	0·659	4·45
0·70	0·946	0·740	5·52
0·80	0·971	0·824	6·94
0·90	0·990	0·910	9·52

* $x_1 = a_1$; $f_1 = f_2 = 1$

n-*Butylamine–benzene–boehmite (Type II)*

x_1 (Bu^nNH_2)	x_1^s	f_1^s	f_2^s
0·10	0·536	0·218	1·97
0·20	0·636	0·365	2·27
0·30	0·694	0·493	2·39
0·40	0·740	0·608	2·44
0·50	0·776	0·728	2·39
0·60	0·810	0·820	2·34
0·70	0·827	0·924	2·04
0·80	0·843	1·02	1·60
0·90	0·868	1·09	1·08

Ethylene dichloride–benzene–γ-Al_2O_3 (Type I)

x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s
0·10	0·187	0·535	1·11
0·20	0·357	0·560	1·24
0·30	0·511	0·587	1·43
0·40	0·645	0·620	1·69
0·50	0·739	0·677	1·92
0·60	0·815	0·736	2·16
0·70	0·876	0·799	2·42
0·80	0·923	0·867	2·60
0·90	0·965	0·933	2·86

Ethyl alcohol–benzene–γ-Al_2O_3 (Type I)

x_1 (EtOH)	x_1^s	f_1^s	f_2^s
0·10	0·703	0·707	3·29
0·20	0·756	0·758	3·92
0·30	0·759	0·832	3·87
0·40	0·788	0·860	4·28
0·50	0·800	0·905	4·36
0·60	0·807	0·934	4·25
0·70	0·836	0·939	4·44
0·80	0·856	0·985	5·35
0·90	0·931	0·985	5·31

n-*Butyl alcohol–benzene–γ-Al_2O_3 (Type I)*

x_1 (Bu^nOH)	x_1^s	f_1^s	f_2^s
0·10	0·667	0·535	2·86
0·20	0·768	0·809	3·89
0·30	0·814	0·950	4·62
0·40	0·845	0·955	5·24
0·50	0·861	0·992	5·52
0·60	0·875	0·976	5·59
0·70	0·919	0·947	7·48
0·80	0·932	0·967	7·10
0·90	0·960	0·971	7·20

n-*Butylamine–benzene–γ-Al_2O_3 (Type II)*

x_1 (Bu^nNH_2)	x_1^s	f_1^s	f_2^s
0·10	0·500	0·234	1·83
0·20	0·600	0·387	2·06
0·30	0·637	0·537	2·01
0·40	0·662	0·680	1·88
0·50	0·675	0·833	1·65
0·60	0·700	0·949	1·48
0·70	0·725	1·05	1·28
0·80	0·753	1·14	1·02
0·90	0·787	1·20	1·18

n-*Butyl alcohol–benzene–γ-$Al(OH)_3$ (Type I)*

x_1 (Bu^nOH)	x_1^s	f_1^s	f_2^s
0·10	0·741	0·482	3·68
0·20	0·756	0·821	3·70
0·30	0·771	1·01	3·75
0·40	0·780	1·03	3·69
0·50	0·803	1·06	3·89
0·60	0·832	1·03	4·16
0·70	0·875	0·99	4·85
0·80	0·925	0·97	6·44
0·90	0·966	0·96	8·32

Ethylene dichloride–benzene–silica gel (Type I)

x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s
0·10	0·158	0·633	1·07
0·20	0·295	0·678	1·13
0·30	0·417	0·719	1·20
0·40	0·524	0·763	1·26
0·50	0·621	0·805	1·32
0·60	0·707	0·849	1·37
0·70	0·786	0·891	1·40
0·80	0·861	0·929	1·44
0·90	0·934	0·964	1·50

Methyl acetate–benzene–silica gel (Type I)

x_1 (MeOAc)	x_1^s	f_1^s	f_2^s
0·10	0·548	0·259	2·12
0·20	0·662	0·432	2·70
0·30	0·762	0·533	3·54
0·40	0·835	0·607	4·58
0·50	0·886	0·676	5·76
0·60	0·920	0·736	6·89
0·70	0·945	0·802	7·63
0·80	0·962	0·874	7·60
0·90	0·982	0·939	8·02

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n-Butylamine–benzene–silica gel (Type I)

x_1 (Bu^nNH_2)	x_1^s	f_1^s	f_2^s
0·10	0·635	0·184	2·51
0·20	0·701	0·331	2·76
0·30	0·743	0·460	2·84
0·40	0·781	0·576	2·89
0·50	0·818	0·687	2·94
0·60	0·854	0·778	3·05
0·70	0·885	0·863	3·06
0·80	0·919	0·936	3·10
0·90	0·956	0·987	3·23

Pyridine–cyclohexane–silica gel (Type I)

x_1 (C_5H_5N)	f_1	f_2	x_1^s	f_1^s	f_2^s
0·10	3·29	1·01	0·824	0·399	5·16
0·20	2·63	1·07	0·892	0·589	7·90
0·30	2·09	1·18	0·920	0·682	10·3
0·40	1·76	1·32	0·931	0·755	11·5
0·50	1·54	1·53	0·939	0·822	12·5
0·60	1·32	1·79	0·944	0·838	12·8
0·70	1·18	2·14	0·959	0·858	15·7
0·80	1·07	2·56	0·970	0·882	17·0
0·90	1·01	3·17	0·979	0·924	15·1

Ethylene dichloride–benzene–titania gel (Type I)

x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s	x_1 $C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s	x_1 ($C_2H_4Cl_2$)	x_1^s	f_1^s	f_2^s
0·10	0·208	0·481	1·14	0·40	0·648	0·617	1·70	0·70	0·914	0·766	3·49
0·20	0·357	0·560	1·24	0·50	0·765	0·654	2·13	0·80	0·957	0·836	4·65
0·30	0·517	0·580	1·45	0·60	0·852	0·704	2·70	0·90	0·983	0·916	5·88

Discussion

Representative data are shown in the Figures, in which surface activity coefficients are plotted against *surface* mole fractions; further data are tabulated. The data fall into two of the three types which were noted previously. For systems which are free from chemisorption, Type I is the commonest, whereas for carbon surfaces Type II was the commonest. The extent to which the two types of surface have been compared is limited, in part, by reaction of some substances with or at the gel surface. Nevertheless, the results reflect the ability of the more polar surfaces of the gels to interact more strongly with polar liquids than can carbon, whereas both types of solid will interact relatively weakly with the less polar liquids. Usually the oxide gels adsorb one liquid preferentially at all concentrations, whereas the carbons show opposite preferences at the two ends of the concentration range. The greater discriminating power of the gels is further shown by the higher values to which they give rise for the surface activity coefficients of the less strongly adsorbed component than for adsorption on carbons.

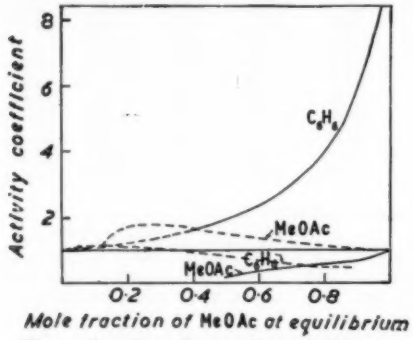
These features are well illustrated by the system methyl acetate–benzene (Fig. 1). With charcoal the system gives Type II curves, the more volatile methyl acetate having a higher surface activity coefficient over most of the concentration range. Methyl acetate thus does not interact with the charcoal surface sufficiently strongly to overcome the effect of its greater volatility with respect to benzene. Boehmite, however, can interact with the polar centre in the methyl acetate molecule strongly enough to adsorb it preferentially from all mixtures with benzene, as it can with methyl acetate–ethylene dichloride. Ethylene dichloride is itself more strongly held than benzene (presumably owing to polarisation of the chlorine atoms) but boehmite still discriminates very sharply between methyl acetate and ethylene dichloride when it is brought into contact with mixtures of the two.

The system ethylene dichloride–benzene has been examined with nearly all of the adsorbents we have studied. With charcoal it gives the rather rare Type III behaviour. With all the gels it gives Type I behaviour, ethylene dichloride being the more strongly adsorbed component. The behaviour of this system is very similar with all the gels, which are differentiated only by the values of the surface-activity coefficients; boehmite and γ-alumina appear as more " active " solids than silica and titania gels.

For the system benzene–*cyclo*hexane, in which the difference in polar character between the two liquids is less, the differences in behaviour between the two types of solid are much less. Although Type I behaviour is found with charcoal, Type II behaviour is found with both graphite [2] and boehmite (Fig. 2).

The chemical reactions which take place at the surface of the gels with a number of the most polar liquids include the catalysed decomposition of some potential adsorbates (*e.g.*,

FIG. 1. *Surface-activity coefficient curves for mixtures of methyl acetate and benzene adsorbed on (a) charcoal and (b) boehmite.*



(Curves for adsorption on charcoal shown as broken lines.)

FIG. 2. *Surface-activity coefficient curves for mixtures of benzene and* cyclo*hexane adsorbed on boehmite.*

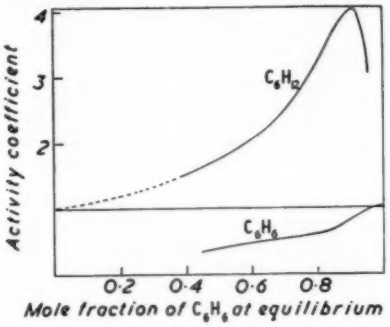


FIG. 3*a*.

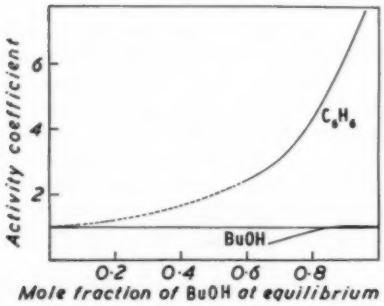


FIG. 3*b*.

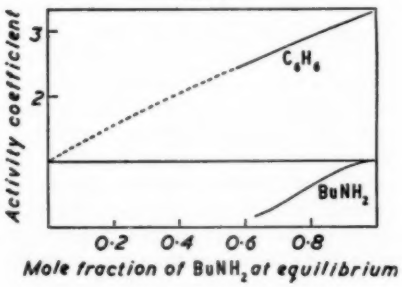


FIG. 3. *Surface activity coefficient curves for (a) mixtures of* n*-butyl alcohol and benzene adsorbed on* γ-Al_2O_3, *(b) mixtures of* n*-butylamine and benzene adsorbed on silica gel.*

FIG. 4*a*.

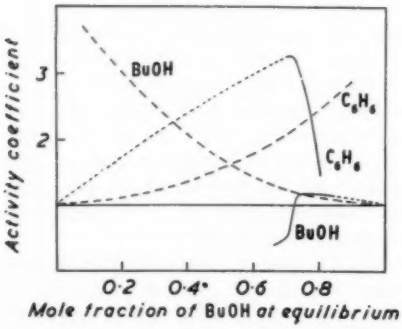


FIG. 4*b*.

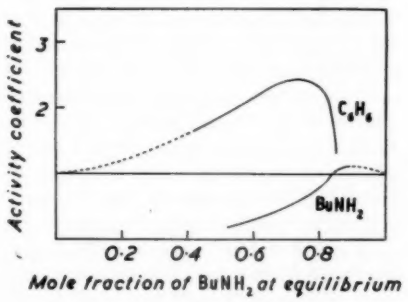


FIG. 4. *Surface activity coefficient curves for (a) mixtures of* n*-butyl alcohol and benzene adsorbed on boehmite (curves for activity coefficients for the liquid phase against liquid phase composition are shown as broken lines), (b) mixtures of* n*-butylamine and benzene adsorbed on boehmite.*

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acetone and *tert.*-butyl chloride in contact with boehmite), the dissolution of boehmite by the lower fatty acids, and the chemisorption of the lower alcohols by oxide groups at the surface.[4] In the last case, physical adsorption of the alcohols from mixtures with benzene may occur on the surface which has been modified by chemisorption. Even on the modified surface the adsorption of the alcohols is so strong that it is difficult to evaluate surface activity coefficients over any considerable range of surface mole fraction, and in the small range available the accuracy is not high. To a less extent, the same applies to adsorption from mixture of nitrogenous bases with hydrocarbons. Nevertheless, from the systems most favourable for calculations, there are indications that both Type I (ethyl alcohol–benzene–γ-Al_2O_3, Fig. 3*a*; *n*-butylamine–benzene–silica gel, Fig. 3*b*) and Type II (*n*-butyl alcohol–benzene–boehmite, Fig. 4*a*; *n*-butylamine–benzene–boehmite, Fig. 4*b*) curves are found.

Two general conclusions may be drawn. When there is no chemisorption, physical adsorption from a given mixture is very similar on all the gels. Furthermore, absolute volatility, which was found in some cases to be important in determining the nature of preferential adsorption on carbon surfaces, has not been found to be important in adsorption on the gels. In all cases the polar nature of the adsorbates is of greater importance, and leads to Type I behaviour in most cases. When the surface is modified by chemisorption, so that it becomes somewhat less polar (chemisorption of alcohols leaves a number of free hydroxyl groups [4]), Type II behaviour is more often observed. This may reflect the dual nature of the surface, part of which is still polar and the remainder non-polar where alkyl groups are bonded to it. Type III behaviour, in which the interaction at the surface is so non-specific that it is of less consequence than interaction between the two components of the liquid, has not yet been observed with these gels.

Experimental

The adsorption [3] and most of the activity data for the bulk liquids have been published.[3] The remainder have been determined from our vapour-pressure data, with the exception of those for the system *n*-butyl alcohol–benzene; for this system we used data [5] for 25°, which therefore apply only approximately to the adsorption data, which were obtained at 20°.

The University, Hull. [*Received, March 19th*, 1958.]

793. *The Kinetics of Hydrogen Isotope Exchange Reactions. Part VIII.* Hydrogen Exchange between Aromatic Compounds and Aqueous Solutions of Weak Acids. Hammett's Acidity Function in Such Solutions.*

By D. P. N. Satchell.

Existing measurements of Hammett's acidity function, H_0, for aqueous solutions of dichloroacetic acid, trifluoroacetic acid, and potassium hydrogen sulphate have been supplemented. Previous data for potassium hydrogen sulphate have been found in error; the acidity scale for it is reproducible and consistent with expectations based on the scales exhibited by other weak inorganic acids. The scale for dichloroacetic acid lacks generality, and no increase in indicator ionisation is observed when small quantities of water are added to the effectively anhydrous acid. This behaviour is discussed in the light of Bruckenstein and Kolthoff's results for acetic acid.

Previous kinetic work in aqueous solutions of weak acids is discussed in connection with the new H_0 data. In particular, Bell and Brown's conclusions, from their study of the decomposition of paraldehyde in aqueous potassium hydrogen sulphate solutions, are revised.

Measurements of the rate of the tritium isotope exchange between nuclear-labelled 1 : 2 : 3-trimethoxybenzene and the aforementioned acidic systems are reported. The pattern of the results is similar to that observed for the decomposition of paraldehyde.

For aqueous solutions of moderately weak acids, relatively few measurements of Hammett's acidity function [1] have been reported.[2] Those which are derived from studies [3,4] with trifluoro- and trichloro-acetic acids, dichloroacetic acid, and potassium hydrogen sulphate are of special interest arising from the fact that, unlike the H_0 values [2] exhibited by other *mineral* acids, both of comparable and greater strengths, they exhibit extensive regions where H_0 appears to change little, if at all, with acid concentration. Few indicators were used in these studies and a tentative, yet attractive, explanation of the behaviour of the *organic* acid solutions, in terms of large specific salting-in effects, has been advanced,[2] but this cannot cover the simple mineral acid potassium hydrogen sulphate, whose reported behaviour therefore appears particularly strange.

Of the many [5] acid-catalysed reactions whose rates are normally governed by H_0, only two, the hydrolysis of sucrose [6] and the decomposition of paraldehyde,[4] have been studied with the weak acids mentioned above. The former reaction in solutions of trichloroacetic acid, and the latter in tri- and di-chloroacetic acid solutions and in solutions of potassium hydrogen sulphate, appear to depart from their usual dependence on H_0: their rates continue to increase when H_0 approaches constancy. Large specific salt effects can again be invoked [5] in explanation for the organic acids but hardly for potassium hydrogen sulphate. The operation of an additional reaction mechanism is an alternative explanation.[4]

To throw more light on these matters, and on the general status of Hammett's function for weak acids, (*a*) the acidity-function measurements for dichloroacetic acid–water mixtures have been extended to cover the entire composition range, (*b*) the more dilute solutions of this acid, and also those of trifluoroacetic acid and potassium hydrogen sulphate, have been studied with additional indicators, and (*c*) an acid-catalysed reaction, namely

* Part VII, *J.*, 1958, 1927.

[1] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co. Inc., New York, 1940.
[2] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[3] Randles and Tedder, *J.*, 1955, 1218.
[4] Bell and Brown, *J.*, 1954, 774.
[5] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.
[6] Hantzsch and Weissberger, *Z. phys. Chem.*, 1927, **125**, 251.

aromatic hydrogen isotope exchange, whose rate is normally controlled by H_0, but which is of a different type from both the sucrose hydrolysis and the paraldehyde decomposition, has been studied in these weakly acidic solutions.

Experimental

Acidity-function Measurements.—These were made, by standard methods,[2,7] with a Beckman spectrophotometer at 23° ± 2°. For all solutions, including the nearly anhydrous region of dichloroacetic acid–water mixtures, ε_B, the maximum extinction coefficient of the basic form of an indicator, was taken to be equal to its value determined in water. In justification of this procedure, weakly basic indicators such as 6-bromo-2 : 4-dinitroaniline in anhydrous dichloroacetic acid, and 4-chloro-2-nitroaniline, *o*-nitroaniline, and *p*-nitrodiphenylamine in acetic acid, showed ε_B in every case to be within *ca.* 4% of the value obtained in water. H_0 was calculated from the best pK_a values given by Paul and Long.[2]

Hydrogen-exchange Experiments.—The level of acidity in solutions of weak acids is necessarily low, so a more reactive aromatic compound than had been studied [8,9] was needed if the exchange rate was to be conveniently measurable at ordinary temperatures. The partial rate factors for anisole,[9] and the known dependence [8] of the aromatic hydrogen exchange rate on H_0, suggested that 1 : 2 : 3-trimethoxybenzene would be suitable, as was found to be so, although it was less reactive than expected.[10] The equivalent positions *ortho* to the 1- and the 3-methoxyl group must be *ca.* 10^5 times more reactive than the remaining 5-position. As before, the exchange was studied as the loss of heavy isotope from the aromatic compound to an excess of light solvent. In other work we have used deuterium, and followed the exchange by infrared analysis. This technique requires a monodeuterated material, and [$^2H_1$]1 : 2 : 3-trimethoxybenzene is not readily accessible. Tritium was therefore used as the label. Tritiated material was prepared (as below) and the rate of loss of tritium to an excess of the acid mixture in question, measured under homogeneous conditions. In these circumstances, the rate constants are of the first order.

The exchange was followed by the same general method for all the acid mixtures. Tritiated compound was dissolved in acid contained in flasks fitted with ground-glass stoppers, and immersed in a thermostat bath at 25°. After known periods samples were withdrawn, diluted with water, and (for trifluoro- and dichloro-acetic acids) neutralised with concentrated cooled sodium hydroxide. (Enough acid mixture to contain *ca.* 0·08 g. of trimethoxybenzene was taken. This weight and the substrate solubility determined the volumes employed. In no case was the substrate concentration allowed to exceed 0·04M.) The neutralised solution was extracted with ether, and the ether extract kept over calcium chloride and a little anhydrous sodium carbonate. Evaporation of the ether left crystalline material of good m. p.

The tritium content of a sample was found by scintillation counting. A weighed amount was dissolved in a scintillation solution containing xylene and the scintillators PPO (2 : 5-diphenyloxazole) and POPOP [1 : 4-di-(5-phenyloxazol-2-yl)benzene]. It was counted with standard equipment. The tritium content of a sample was thus compared with that of the original material, and the exchange followed. Good first-order exchange rate constants (λ) were obtained (Tables 4, 5, and 6).

Materials.—(*a*) Potassium hydrogen sulphate of highest available commercial purity was used. Both the crystalline and fused products were employed. (*b*) Pure dichloroacetic acid decomposes with time. An aged sample, diluted with water, gave a faint white precipitate with silver nitrate. "Purified" commercial samples also reacted in this way. Reasonably anhydrous material (0·05M-water by Karl Fischer titration), which gave no precipitate with silver nitrate, was prepared by a preliminary drying ($CaSO_4$) followed by vacuum distillation at 1—2 mm. Aged samples were redistilled at this pressure before use. (*c*) Trifluoroacetic acid was as supplied by Columbia Organic Chemicals Ltd. (*d*) *p*-Nitroaniline, *o*-nitroaniline, 4-chloro-2-nitroaniline, diphenylamine, and *p*-nitrodiphenylamine were recrystallised samples of m. p. 148°, 71·6°, 116°, 54°, and 135° respectively. (*e*) 1 : 2 : 3-Trimethoxybenzene, m. p. 46°, was prepared by Olivero and Bargellini's method [11] from pyrogallol. It was tritiated by

[7] Satchell, *J.*, 1958, 1916.
[8] Gold and Satchell, *J.*, 1955, 3609.
[9] Satchell, *J.*, 1956, 3911.
[10] Satchell, to be published.
[11] Olivero and Bargellini, *Gazzetta*, 1948, **78**, 372.

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dissolving it in an acidified 24·4 moles % ethanol–water mixture, of known [13] H_0, containing tritiated water. After an appropriate interval, based on the expected exchange rate at 25°, the mixture was neutralised with sodium hydroxide and diluted with water, thus precipitating the product. This was well washed with water and dried. Tests for incomplete methylation were negative, and tritiated material dissolved in ethanol–water and immediately re-isolated suffered a negligible change in activity. The observed counting rate indicated that exchange equilibrium was incompletely established at the 4- and the 6-position. Exchange at the 5-position should, therefore, have been negligible, as was confirmed by the linearity of the first-order plots.

TABLE 1(*a*). *Acidity function in dichloroacetic acid–water mixtures as determined by* (a) p-*nitroaniline*, (b) *diphenylamine*, (c) o-*nitroaniline*, (d) 4-*chloro*-2-*nitroaniline*, *and* (e) p-*nitrodiphenylamine*.

$CHCl_2{\cdot}CO_2H$ (M) ...	0·05	0·12	0·24	0·48	1·21	2·42	4·84
H_0 by (a)	1·50	1·18	0·95	0·75	0·61	0·60	0·60
H_0 by (b)	1·52	1·21	0·99	0·76	0·56	0·35	−0·05
H_0 by (c)	—	—	—	—	0·66	0·64	0·64
$CHCl_2{\cdot}CO_2H$ (M) ...	7·26	8·47	9·68	10·16	10·89	12·13	
H_0 by (a)	0·38	0·17	−0·35	—	—	—	
H_0 by (c)	0·50	—	−0·20	−0·39	−0·74	—	
H_0 by (d)	—	0·40	−0·10	−0·22	−0·56	−0·74	
H_0 by (e)	—	—	—	−0·97	−1·26	−1·57	

TABLE 1(*b*). *Effect of added water on the acidity of nearly anhydrous dichloracetic acid* (0·05M-H_2O) *as indicated by* (a) 4-*chloro*-2-*nitroaniline and* (b) p-*nitrodiphenylamine*.

Total H_2O (M) ...	0·05	0·14	0·24	0·61	1·05	1·84	3·52	5·05
H_0 by (a)	−0·74	−0·74	−0·73	−0·72	—	−0·70	−0·65	−0·60
H_0 by (b)	−1·57	−1·57	−1·56	—	−1·54	—	−1·46	−1·40

TABLE 2. *Acidity function in potassium hydrogen sulphate–water mixtures as determined by* (a) p-*nitroaniline*, (b) *diphenylamine*, *and* (c) o-*nitroaniline*.

$KHSO_4$ (M)	0·25	0·50	1·00	1·50	2·00	2·25
H_0 by (a)	0·96	0·66	0·35	0·15	−0·03	−0·14
H_0 by (b)	—	0·70	0·38	0·15	−0·01	—
H_0 by (c)	—	0·67	0·34	0·12	−0·04	−0·15

TABLE 3. *Acidity function in trifluoroacetic acid–water mixtures as determined by* (a) o-*nitroaniline*, *and* (b) *diphenylamine*.

$CF_3{\cdot}CO_2H$ (M)	0·99	2·16	4·04	5·39	6·73
H_0 by (a)	0·09	−0·12	−0·28	−0·42	−0·64
H_0 by (b)	0·24	−0·07	−0·19	−0·37	—

TABLE 4. *Rate of loss of tritium from* [4 : 6-^{3}H]1 : 2 : 3-*trimethoxybenzene in aqueous potassium hydrogen sulphate at* 25°.

$KHSO_4$ (M)	0·50	1·00	2·00	2·50
$10^7\lambda$ (sec.$^{-1}$)	1·84	4·41	10·5	14·4

TABLE 5. *Rate of loss of tritium from* [4 : 6-^{3}H]1 : 2 : 3-*trimethoxybenzene in aqueous dichloroacetic acid at* 25°.

$CHCl_2{\cdot}CO_2H$ (M)	0·12	0·24	1·21	2·42	4·84	7·24	12·13
$10^7\lambda$ (sec.$^{-1}$)	0·34	0·48	1·51	2·40	6·0	11·0	1230

TABLE 6. *Rate of loss of tritium from* [4 : 6-^{3}H]1 : 2 : 3-*trimethoxybenzene in aqueous trifluoroacetic acid at* 25°.

$CF_3{\cdot}CO_2H$ (M)	0·99	2·16	4·04	6·73
$10^7\lambda$ (sec.$^{-1}$)	4·80	12·2	49·8	137

RESULTS AND DISCUSSION

Acidity Functions.—(a) *Dichloroacetic acid–water mixtures.* The only previous data for this system are those of Bell and Brown.[4] They used one indicator, *p*-nitroaniline,

[13] Satchell, *J.*, 1957, 3524.

and dichloracetic acid concentrations below 5M. The results given in Table 1 were obtained with five indicators, and cover the composition range from *ca.* 0·05M to the almost anhydrous acid (12·1M-acid, 0·05M-water). The region close to the pure acid was studied in some detail.

Several points of interest emerge. In the dilute acid region (below 5M) the values for *p*-nitroaniline agree only moderately well with Bell and Brown's. 0·99 being used as pK_a of *p*-nitroaniline, the present values lie *ca.* 0·1 unit above Bell and Brown's at 4M and fall off more slowly at lower acidities. The data for *o*-nitroaniline agree well with the new values for *p*-nitroaniline. The same is true for diphenylamine at acid concentrations below 0·5M. However, above this point diphenylamine indicates a continued rise in acidity and does not show the H_0 plateau exhibited by *p*- and *o*-nitroaniline between *ca.* 1M and 3M. These findings support Paul and Long's suggestion [2] that appreciable salting-in of indicators by the organic acid is responsible for the H_0 plateau, and that indicators of different structural type should show specific effects. Thus *p*- and *o*-nitroaniline behave much the same, whereas diphenylamine exhibits divergent behaviour when the acid concentration becomes appreciable.

The more concentrated region (above 5M) has been covered with the indicators *o*-nitroaniline, 4-chloro-2-nitroaniline, and *p*-nitrodiphenylamine. Above *ca.* 5M there is no agreement at all between the data produced by these indicators, though between 7M and 11M their trends are similar. Some change in behaviour is expected [7] in view of the alteration in the character of the medium, from one of high to one of low dielectric constant, which is occurring. Changes in the relative basicities of the indicators are expected,[7] and in the effectively anhydrous solvent 4-chloro-2-nitroaniline gives $H_0 = -0{\cdot}74$ in comparison with $-1{\cdot}57$ given by *p*-nitrodiphenylamine. Similar discrepancies occur in the literature concerning anhydrous trifluoroacetic acid.[13] Too much weight is not, however, to be attached to the absolute values of H_0 in the nearly anhydrous region, since determinations seemed somewhat dependent on impurities other than water.

The present results for dichloroacetic acid imply that, at least for aqueous solutions, the H_0 scale for this weak acid is not useful: it is not independent of the indicator used in its determination.

A final point of interest concerns the almost anhydrous region. Bruckenstein and Kolthoff [14] have shown that with acetic acid, indicators which are partly ionised in the anhydrous solvent become more so on the addition of small quantities of water—a base in this medium. They explain the phenomenon by the formation of triple and quadruple ions, involving protonated water molecules. Although these authors did not carry their experiments so far, there must come a time, as more water is added, when its effect as a base in lowering the overall acidity of the medium begins to outweigh its effect in promoting ion association. Thus, with suitable indicators, an acidity maximum should be observed in acetic acid. Since the dielectric constants of acetic and dichloroacetic acids are not very different, a similar phenomenon might be expected in the latter. The relevant data in Table 1(*b*), although not very accurate, imply that no maximum exists, although the decrease in acidity on addition of water is at first very slow. The reason for the absence of the marked effects shown in acetic acid is probably to be found in the greater strength of the substituted acid. The addition of water will have a much more pronounced effect on the acidity, and its rôle as a base will, therefore, quickly become dominant.

(b) *Potassium hydrogen sulphate–water mixtures.* The previous data here are again those of Bell and Brown,[4] who used *p*-nitroaniline, and acid concentrations up to 2·7M. The values for *p*-nitroaniline have now been redetermined, and measurements made with diphenylamine and *o*-nitroaniline over the same concentration range (Table 2). The previous authors found an H_0 plateau above *ca.* 1M. In the present study no such region has been found, but rather a general increase in acidity with concentration. Furthermore,

[13] Kilpatrick and Hyman, *J. Amer. Chem. Soc.*, 1958, **80**, 77; Van Dijke Tiers, *ibid.*, 1956, **78** 4165.
[14] Bruckenstein and Kolthoff, *J. Amer. Chem. Soc.*, 1956, **78**, 10.

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all three indicators give values which are in very reasonable mutual agreement. The behaviour now exhibited is that expected from aqueous solutions of a relatively weak inorganic acid. It is concluded that the H_0 scale for solutions of potassium hydrogen sulphate is useful, for it seems very likely that other indicators will also give values in agreement with these now obtained. The position of this acid, among weak acids in general, no longer appears anomalous. In Fig. 1 the data are compared with those for hydrogen fluoride and phosphoric acid in the same concentration region.[2] Potassium hydrogen sulphate takes its proper place, being slightly stronger than phosphoric acid.

(c) *Trifluoroacetic acid–water mixtures.* Randles and Tedder[3] studied this system using *o*- and *p*-nitroaniline and 4-chloro-2-nitroaniline. Measurements with *o*-nitroaniline give values in reasonable agreement with theirs (Table 3). Diphenylamine gives data which are, on the average, 0·09 unit more positive, but which, in contrast to the behaviour shown in dichloroacetic acid, show no marked tendency to decrease rapidly with increasing acid concentration. The change in indicator structure involved thus has less effect on the reproducibility of the H_0 scale in this case.

FIG. 1. *Acidity functions for weak acids* (*a*) HF, (*b*) H_3PO_4, (*c*) $KHSO_4$.

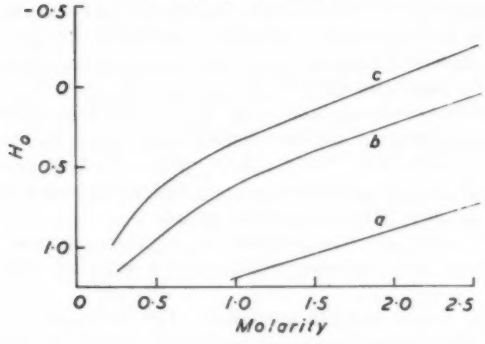
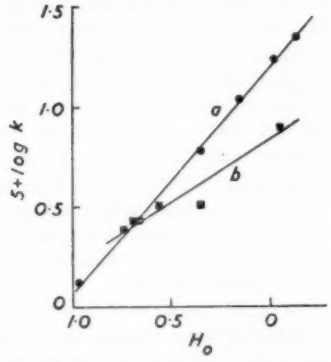


FIG. 2. *Decomposition of paraldehyde in weak acids* (*a*) $KHSO_4$, (*b*) $CHCl_2{\cdot}CO_2H$.



Previous Studies of Acid Catalysis in Solutions of Weak Acids.—There have been only two such studies in which correlations between rates and H_0 were to be expected. These concern (*a*) the decomposition of paraldehyde, and (*b*) the hydrolysis of sucrose.

(*a*) The paraldehyde decomposition was studied by Bell and Brown[4] who used aqueous solutions of potassium hydrogen sulphate and of dichloro- and trichloro-acetic acids. They showed that in the common aqueous mineral acids the rate of decomposition is controlled by H_0 but that for the above three acids the rate appeared to increase faster than H_0 required. However, for potassium hydrogen sulphate a plot (Fig. 2) of their rate constants against the amended acidity data gives a very good straight line of slope 1·12, in close agreement with that found for the other mineral acids. The mechanism of the paraldehyde decomposition in aqueous hydrogen sulphate is thus identical with that obtaining in solutions of the other inorganic acids, and there is no discrepancy in need of explanation, either in terms of salt effects or of additional reaction paths.

For dichloroacetic acid the decomposition rates do not correlate badly with the amended H_0 data for *p*-nitroaniline, apart from the last point. They increase *less* rapidly than the data for diphenylamine demand (Fig. 2). Bearing the lack of generality of the acidity scale for dichloroacetic acid in mind, we see that there is no clear evidence of a lack of dependence of rate on H_0. The reaction mechanism in this medium seems very likely to be much the same as in aqueous solutions of inorganic acids.

It is thus only trichloroacetic acid for which any problem remains. Here there exists

a real divergence between existing H_0 data and reaction rate. Further discussion is deferred.

(*b*) The rate of hydrolysis of sucrose, which correlates with H_0 in aqueous mineral acids, also fails to do so in aqueous trichloroacetic acid, the only weak acid in which the reaction has been studied.[5]

Aromatic Hydrogen Isotope Exchange.—(a) *Status of the reaction.* The acid-catalysed decomposition of paraldehyde can be accomplished by Lewis, as well as by Brønsted acids.[15] The fact that the reaction is, in essence, only an electronic rearrangement, suggests that it may be particularly prone to catalysis by a variety of paths. The acid-catalysed hydrolysis of sucrose is complex, and may also be particularly susceptible to catalysis by more than one route. Both these reactions must involve electrophilic attack on oxygen when the catalyst is a Brønsted acid.

Aromatic hydrogen isotope exchange was chosen for this study because the acid-catalysed process is relatively simple, and must involve Brønsted acids. The electrophilic attack is also on carbon, rather than on oxygen. The reaction is thus of a different type from the two previously studied in these solvents.

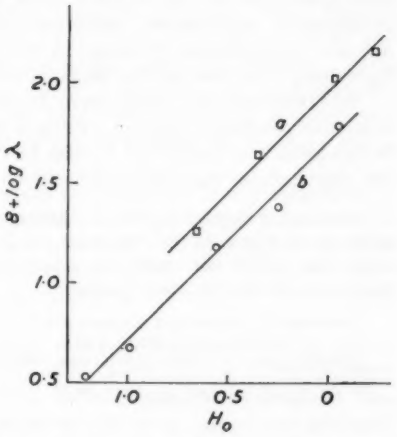


FIG. 3. *Hydrogen isotope exchange in weak acids* (*a*) $KHSO_4$, (*b*) $CHCl_2{\cdot}CO_2H$.

In aqueous solutions of the mineral acids the exchange rate follows H_0 for all the aromatic compounds so far studied,[16] including trimethoxybenzene.[10] Correlation is exhibited also in solutions of such acids in anhydrous acetic [9] and trifluoroacetic acid.[17] Whether the mechanism, under these conditions, involves a rapid pre-equilibrium followed by a rate-determining rearrangement of the conjugate acid of the aromatic compound or, alternatively, a slow proton transfer, is still debated.[5]

(b) *Potassium hydrogen sulphate–water mixtures.* Four different mixtures were studied covering the range 0·5—2·5M. The first-order exchange rate constants are collected in Table 4. Plotted against the appropriate H_0 values * (Fig. 1) they produce a good straight line of slope 1·02 (Fig. 3). This correlation is to be expected in view of the behaviour of the paraldehyde decomposition previously discussed. It seems that potassium hydrogen sulphate–water mixtures will prove suitable media for experiments

* For these acid mixtures, as for the others discussed below, measurements were made of the effect of the dissolved trimethoxybenzene on the value of H_0. In all cases the acidity was decreased. For potassium hydrogen sulphate solutions the change was negligible. For the other solutions the change was larger (though in no case greater than 0·1 unit) but sufficiently constant for no significant error to be introduced by using the data given in Tables 1 and 3.

[15] Bell and Skinner, *J.*, 1952, 2955.
[16] Gold and Satchell, *J.*, 1955, 3619; see also refs. 8 and 9.
[17] Mackor, Smit, and van der Waals, *Trans. Faraday Soc.*, 1957, **53**, 1309.

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of the Zucker–Hammett design,[5] always provided that general acid-catalysed reaction rates do not fortuitously correlate with H_0 also. This point remains to be established.

(c) *Dichloroacetic acid–water mixtures.* Seven mixtures, with acid contents ranging from 0·1 to 7·3M, were used, and the rate was also measured in the anhydrous solvent. The rate constants are collected in Table 5, and plotted against H_0, as measured by diphenylamine, in Fig. 3. The correlation is fairly good. The rate in the anhydrous solvent is also roughly what one might expect on the basis of the data in Table 1. There is clearly no marked departure from correlation with indicator ionisation. This finding is again in keeping with the behaviour of paraldehyde. The fact that the exchange rates in aqueous dichloroacetic acid and potassium hydrogen sulphate are not quite the same at the same value of H_0 was rather to be expected in view of previous work.[18]

(d) *Trifluoroacetic acid–water mixtures.* Acid catalysis in this system does not appear to have been studied previously. Four mixtures were used varying from 1·0 to 6·7M-acid, *i.e.*, covering the H_0 plateau region. The exchange rate constants are given in Table 6. In this system, as found previously for trichloroacetic acid, the reaction rate increases faster than existing H_0 data demand. These, while admittedly very limited, indicate some generality for the function, so it appears likely that some additional, and probably synchronous, mechanism, involving catalysis by the un-ionised organic acid molecule operates for hydrogen exchange in trifluoroacetic acid solutions, and possibly also for the hydrolysis of sucrose and the decomposition of paraldehyde in trichloroacetic acid solutions.

Whether any such mechanism is important for these reactions in dichloroacetic acid is not yet possible to decide. There is still no need to postulate one. In any case, it will be rendered less prominent by the fact that the hydrogen atom of dichloroacetic acid is less electrophilic than those of trichloro- and trifluoro-acetic acids.

The author thanks Dr. D. R. Christman for advice and help in connection with the tritium analyses, and Drs. R. W. Stoenner and J. K. Rowley for help with inorganic analyses. This work was carried out under the auspices of the U.S. Atomic Energy Commision during the tenure of a Research Associateship.

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[18] Gold and Satchell, *J.*, 1955, 3622.

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794. *Indicator Measurements and Hydrogen Isotope Exchange in the Solvent Systems* $SnCl_4$–$CH_3{\cdot}CO_2H$ *and* $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$.

By D. P. N. Satchell.

The ionisation of basic indicators in the systems mentioned in the Title for stannic chloride concentrations below *ca.* 3M is described. The rate of aromatic hydrogen isotope exchange has also been measured. Taken together, the results imply that the acidity exhibited is of the Brønsted–Lowry variety.

The complex acid $H_2SnCl_4(OAc)_2$, which is the active species in the $SnCl_4$–$CH_3{\cdot}CO_2H$ system, is of comparable strength with sulphuric acid. In the presence of hydrogen chloride additional complex formation occurs. The acidic properties of the two systems are compared with those of the analogous systems containing zinc chloride.

The acidity exhibited by systems containing both Lewis and Brønsted acids has only once been quantitatively studied,[1] namely in solutions of zinc chloride, and zinc chloride and hydrogen chloride, in acetic acid. The present work deals with stannic chloride and hydrogen chloride solutions in the same solvent. As before, the nature of the acidity has

[1] Bethell, Gold, and Satchell, *J.*, 1958, 1918.

been examined with the aid of basic indicators and the aromatic hydrogen isotope exchange reaction.[1,2]

Stannic chloride dissolved easily in acetic acid, with the evolution of heat, and mole fractions up to *ca.* 0·4 can be obtained. Thereafter the system forms two layers.[3] There is no evidence of solvolysis, but good reason [4] for believing that a complex of composition $(CH_3{\cdot}CO_2H)_2,SnCl_4$ is formed between the two components, according to the equilibrium

$$2CH_3{\cdot}CO_2H + SnCl_4 \rightleftharpoons (CH_3{\cdot}CO_2H)_2,SnCl_4 \quad . \quad . \quad . \quad . \quad (1)$$

This is the logical complex to expect, involving as it does six-fold co-ordination. This compound is thought to behave as a complex Brønsted acid,[4] and appears to be more or less quantitatively solvated by a further molecule of acetic acid, giving the complex $(CH_3{\cdot}CO_2H)_3,SnCl_4$ whose solutions possess marked electrical conductivity.[3,4] The position of the equilibrium (1) therefore seems to be far to the right.

These findings are in keeping with those for solutions of zinc chloride. For these a similar complex, $(CH_3{\cdot}CO_2H)_2,ZnCl_2$, is considered to exist. (The usual co-ordination number of zinc is four.) It has been shown to behave as a weak Brønsted acid, and to emphasise this property the formula can be written as $H_2ZnCl_2(OAc)_2$. Since stannic chloride is a much stronger Lewis acid than is zinc chloride, the complex between the former compound and acetic acid should be much more acidic than $H_2ZnCl_2(OAc)_2$. The solvent molecules are doubtless complexed *via* the carbonyl oxygen atom, and with the more powerful electrophil stannic chloride there will be a greater drain on the electrons of the oxygen–hydrogen bond, *i.e.*, the ion $[SnCl_4(OAc)_2]^{2-}$ is likely to be more stable than $[ZnCl_2(OAc)_2]^{2-}$.

The expectation of greater strength for the complex acid of tin is clearly confirmed by the apparently quantitative formation of the compound $(CH_3{\cdot}CO_2H)_3,SnCl_4$, for this seems to imply the complete ionisation of one proton of $H_2SnCl_4(OAc)_2$. The marked conductivity also implies appreciable dissociation of the ion pair $[CH_3{\cdot}CO_2H_2]^+[HSnCl_4(OAc)_2]^-$. The strength of the complex stannic acid is estimated from the experiments now to be described.

Indicator Ionisation.—(i) $SnCl_4$–$CH_3{\cdot}CO_2H$ *solvent system.* The ionisation of five of the indicators usual in acidity-function studies,[5] namely, *p*-nitroaniline, *o*-nitroaniline, 4-chloro-2-nitroaniline, *p*-nitrodiphenylamine, and 2 : 4-dichloro-6-nitroaniline, was investigated. These indicators are negligibly ionised in the pure, anhydrous solvent.[1] As increasing amounts of stannic chloride are added to a solution of one of these compounds in acetic acid, the ultraviolet absorption spectrum gradually changes from that characteristic of the basic form of the indicator to that characteristic of the acidic, or ionised, form, as produced by typical Brønsted acids like sulphuric. Measurement of indicator ionisation ratios, I (= ratio of the concentration of ionised to un-ionised form), at various stannic chloride concentrations is thus possible.

The presence of the complex Brønsted acid being assumed, part, at least, of the change in ionisation must be due to it. However, the spectra of the indicators involved are also affected by the addition of small quantities of stannic chloride to their solutions in solvents, such as hexane, with which the stannic chloride will have little chance of forming complexes, and in which, therefore, free Lewis acid will exist. Hence any free stannic chloride which existed in acetic acid would also presumably affect the indicators. To be reasonably sure that the ionisation ratios only reflect the enhanced Brønsted acidity it is necessary to show that, for instance, the rate of some reaction which can only be catalysed by Brønsted acids parallels the changes in ionisation in the way expected. Aromatic hydrogen isotope exchange is a reaction whose rate is usually linear with the extent of ionisation of indicator

[1] Satchell, *J.*, 1958, 1927.
[3] Stranathan and Strong, *J. Phys. Chem.*, 1927, **31**, 1420.
[4] Usanovich and Kalabanovskaya, *Zhur. obshchei Khim.*, 1947, **17**, 1235.
[5] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.

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bases.[6] In the present instance the rates of exchange between *p*-deuteroanisole and the solvent systems have been measured. The experiments are described subsequently. The results imply that the ionisation ratios, in fact, reflect only a Brønsted acidity.

The ionisation data for the indicators, at various stannic chloride concentrations, are collected in Table 1. Their main points of interest are the following. (*a*) The general

TABLE 1. *Ionisation of* (a) p-*nitroaniline*, (b) o-*nitroaniline*, (c) 4-*chloro*-2-*nitroaniline* (d) p-*nitrodiphenylamine, and* (e) 2 : 4-*dichloro*-6-*nitroaniline in solutions of stannic chloride in acetic acid at* 23 ± 2°.

$SnCl_4$ (M)	0·000035	0·00007	0·00014	0·00028	0·00054	0·00089	0·00178	
log I_a	−1·02	−0·69	−0·16	0·26	0·62	0·87	1·27	
log I_b	—	—	—	−1·44	−1·09	−0·79	−0·44	
log I_b − log I_a	—	—	—	−1·70	−1·71	−1·66	−1·71	
$SnCl_4$ (M)	0·00356	0·00534	0·00890	0·0160	0·0267			
log I_b	−0·07	0·26	0·58	1·00	—			
log I_c	−1·05	−0·72	−0·42	−0·03	0·30			
log I_c − log I_b	−0·98	−0·98	−1·00	−1·03	—			
$SnCl_4$ (M)	0·0445	0·0710	0·0889	0·142				
log I_c	0·54	0·83	0·95	1·23				
log I_d	−1·01	−0·71	−0·60	−0·33				
log I_d − log I_c	−1·55	−1·54	−1·55	−1·56				
$SnCl_4$ (M)	0·231	0·356	0·712	0·856	1·14	1·43	2·14	2·86
log I_d	−0·08	0·16	0·53	0·85	—	—	—	—
log I_e	−1·17	−0·92	−0·55	−0·25	−0·19	0·34	0·56	1·17
log I_e − log I_d	−1·09	−1·08	−1·08	−1·10	—	—	—	—

increase in ionisation with stannic chloride concentration is very similar in form to that observed when hydrogen chloride,[7] sulphuric acid,[8] or zinc chloride [1] is added to acetic acid. Fig. 2 shows the data for 4-chloro-2-nitroaniline. (*b*) For hydrogen chloride,[7] sulphuric acid,[5,8] and zinc chloride [1] solutions in acetic acid, the plots of log *I* against the acid concentration for different indicators give curves with fairly constant separations. For any two indicators the exact separations may depend on the acid involved. The separations are also often different from those found when the solvent is water. These discrepancies imply different relative basicities for the indicators under different conditions.[7,9,10]

In the $SnCl_4$–$CH_3{\cdot}CO_2H$ system indicators show similar behaviour to that just described. Table 1 shows that plots of log *I* against stannic chloride concentration would show reasonably constant separations. If the separations be taken to represent the relative basicities of the indicators [7] then ΔpK_a between *p*-nitroaniline and *o*-nitroaniline, between *o*-nitroaniline and 4-chloro-2-nitroaniline, between 4-chloro-2-nitroaniline and *p*-nitrodiphenylamine, and between *p*-nitrodiphenylamine and 2 : 4-dichloro-6-nitroaniline are −1·70, −1·00, −1·55, and −1·09 respectively. The values for water are −1·28, −0·74, −1·45, and 0·84 respectively.[5] Such discrepancies are now becoming a commonplace and emphasise the dependence of relative basicity on medium. For zinc chloride in acetic acid [1] ΔpK_a for the first three of the above pairs are −1·66, −0·95, and −1·22 respectively; the relative basicities seem, in each case, a little greater in the $SnCl_4$–$CH_3{\cdot}CO_2H$ system. (*c*) In Fig. 1 plots of the ionisation of 4-chloro-2-nitroaniline for various zinc chloride, stannic chloride, hydrogen chloride, and sulphuric acid concentrations in acetic acid are compared. Whereas at the same concentrations zinc chloride produces a much less acidic system than does hydrogen chloride, stannic chloride produces an effect comparable with, or greater than, that produced by sulphuric acid. The acid strength of $H_2SnCl_4(OAc)_2$ must therefore be considered comparable with that of sulphuric

[6] Satchell, *J.*, 1956, 3911; and references therein.
[7] Satchell, *J.*, 1958, 1915.
[8] Paul and Hammett, *J. Amer. Chem. Soc.*, 1936, **58**, 2182; Gold and Hawes, *J.*, 1951, 2102.
[9] Roček, *Chem. Listy*, 1956, **50**, 726.
[10] Satchell, *J.*, 1957, 3524.

acid, though in systems like these relative acidity depends to some extent on the base involved. Since previous experiments [3,4] probably indicate that one molecule of solvent

TABLE 2. *Ionisation of* (a) *4-chloro-2-nitroaniline and* (b) *p-nitrodiphenylamine in acetic acid containing both hydrogen chloride and stannic chloride at* 23° ± 2°.

(i) HCl (M) = 0·0115								
$SnCl_4$ (M)	0·0017	0·0033	0·0049	0·0066	0·0083	0·0149	0·033	0·066
log I_a	−0·36	−0·02	0·15	0·24	0·37	0·52	0·91	1·21
(ii) HCl (M) = 0·115								
$SnCl_4$ (M)	0·0083	0·0149	0·042	0·083	0·165	0·346	0·692	1·38
log I_b	−0·74	−0·53	−0·35	−0·05	0·22	0·43	0·71	1·18

is associated with each molecule of $H_2SnCl_4(OAc)_2$, it is reasonable to assume the complete ionisation of one proton. By analogy sulphuric acid must also be fairly completely ionised in acetic acid.

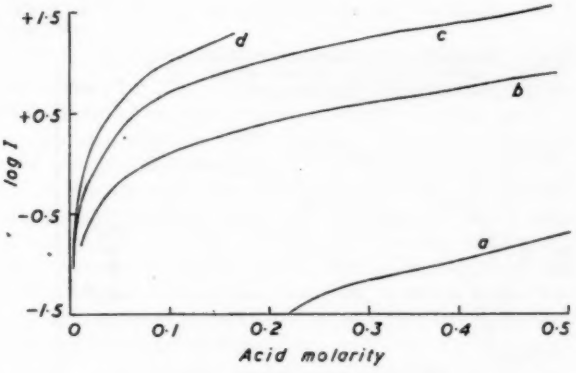


FIG. 1. *Ionisation of 4-chloro-2-nitroaniline in acetic acid containing other acids:* (*a*) $ZnCl_2$, (*b*) HCl, (*c*) H_2SO_4, (*d*) $SnCl_4$.

(ii) $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$ *solvent system.* Two series of measurements were made also of the change in indicator ionisation when increasing quantities of stannic chloride were added to acetic acid containing a constant amount of hydrogen chloride. The first at 0·0115M-hydrogen chloride used 4-chloro-2-nitroaniline and the second at 0·115M-hydrogen chloride used *p*-nitrodiphenylamine (Table 2). A plot of the results obtained at 0·0115M is given in Fig. 2 where log *I* is compared with those obtained with the same indicator in the absence of hydrogen chloride.

A definite increase in acidity is found in the presence of hydrogen chloride, but the marked effects found in the $ZnCl_2$–HCl–$CH_3{\cdot}CO_2H$ system [1] are absent. In the latter system the acidity increases much more for a given hydrogen chloride concentration, and also passes through a maximum value as the zinc chloride concentration is increased. In explanation two further complex Brønsted acids, besides $H_2ZnCl_2(OAc)_2$, have been suggested, namely H_2ZnCl_4 and $H_2ZnCl_3(OAc)$. Of these three species, H_2ZnCl_4 is much the most powerful acid. Its initial formation and subsequent replacement by $H_2ZnCl_3(OAc)$ as the zinc chloride concentration becomes large explains the marked increase in acidity and the acidity maximum.

It was hardly possible to predict whether exactly the same effects would be exhibited by the $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$ system. Fig. 2 reveals that, in fact, they are not. However, it seems very likely that hydrogen chloride and stannic chloride will combine in suitable solvents, though a medium capable of solvation is probably required. As previously mentioned the favoured co-ordination number is likely to be six. For the $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$ system there are, therefore, as for the zinc chloride system, two obvious possibilities besides $H_2SnCl_4(OAc)_2$, namely H_2SnCl_6 and $H_2SnCl_5(OAc)$.

Fig. 2 reveals that though acidity increases when hydrogen chloride is present (an increase much greater than that to be expected were the hydrogen chloride and stannic chloride to operate independently, so that additional complex formation must be assumed), yet it does not reach a maximum as the stannic chloride concentration rises. The explanation lies, very probably, in the greater strength of $H_2SnCl_4(OAc)_2$ than of $H_2ZnCl_2(OAc)_2$.

When stannic chloride is added in deficit to hydrogen chloride in acetic acid, the species H_2SnCl_6 is probably preferentially formed. As more stannic chloride is added two possibilities exist. Either the formation of H_2SnCl_6 will be completed, followed by the formation of $H_2SnCl_4(OAc)_2$, or the initial H_2SnCl_6 may be replaced by $H_2SnCl_5(OAc)$, this being followed by the production of $H_2SnCl_4(OAc)_2$. (The effects will, of course, be of the mass-law type, and will not be as sharply distinct as implied in the preceding sentence.) In either case (and the present experiments cannot decide between them,

FIG. 2. *Ionisation of 4-chloro-2-nitroaniline in the* $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$ *solvent system*: (□) [HCl] = 0·0115M, (△) *without* HCl.

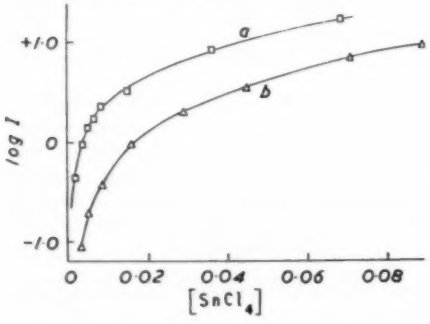
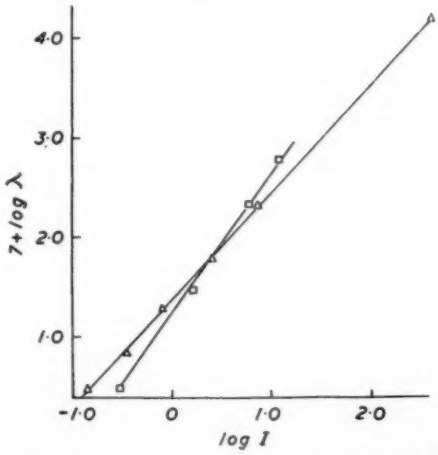


FIG. 3. *Aromatic hydrogen isotope exchange in the* $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$ *solvent system*: (□) [HCl] = 0·115M, (△) *without* HCl.



though the latter scheme seems the more likely) the difference in acidity between H_2SnCl_6 and the other species is likely to be very much less than for the corresponding zinc compounds, for, as we have seen, $H_2SnCl_4(OAc)_2$ is itself highly ionised. Thus it is quite understandable that no maximum should be exhibited in the presence of hydrogen chloride, for even if H_2SnCl_6 is replaced by $H_2SnCl_5(OAc)$ as stannic chloride is added, it is probable that the loss of acidity involved will be more than compensated by the $H_2SnCl_4(OAc)_2$ which must also simultaneously be formed.

Hydrogen isotope exchange reaction. To demonstrate that the observed ionisation ratios were really reflecting only the Brønsted, and not also the Lewis, acidity of the systems, the rate of hydrogen isotope exchange between *p*-deuteroanisole and the various media was studied. This reaction must reflect primarily the Brønsted acidity. For systems which possess only this type of acidity, a large body of previous work [6,11] shows that a plot of the logarithm of the first-order exchange rate constant (λ) against log I customarily provides a straight line with a slope close to unity. (A slope of *ca.* 1·15 appears usual for anisole.[6])

The exchange data are collected in Tables 3 and 4. In Fig. 3 log λ is plotted against log I for *p*-nitrodiphenylamine. The graph for the solutions of stannic chloride alone is

[11] Mackor, Smit, and van der Waals, *Trans. Faraday Soc.*, 1957, **53**, 1309.

an excellent straight line of slope 1·12. The plot in the presence of hydrogen chloride has a greater slope, *viz.*, 1·40. This is in keeping with the results for the $ZnCl_2$–HCl–$CH_3{\cdot}CO_2H$ system, where the exchange rate also increases somewhat more rapidly than the indicator ionisation demands.[2] When more than one acidic species is active in the solvent such behaviour is to be expected, since under such conditions the ionisation ratios for different

TABLE 3. *Hydrogen isotope exchange between* p-*deutero-anisole and the* $SnCl_4$–$CH_3{\cdot}CO_2H$ *system at* 25°.

$SnCl_4$ (M)	0·059	0·118	0·22	0·596	0·879	2·90
$10^7\lambda$ (sec.$^{-1}$) ...	3·01	7·10	19·5	63·1	211	15,900
log I *	−0·85	−0·45	−0·10	0·40	0·86 †	2·30 †

TABLE 4. *Hydrogen isotope exchange between* p-*deutero-anisole and the* $SnCl_4$–HCl–$CH_3{\cdot}CO_2H$ *system at* 25° ([HCl] = 0·115M).

0·015	0·147	0·732	1·10
3·05	29·8	225	617
−0·53	0·20	0·78	1·27

* For *p*-nitrodiphenylamine.
† Extrapolated values, the data for 2 : 4-dichloro-6-nitroaniline being borne in mind.

bases are unlikely to run particularly parallel, and relative basicities are unlikely to remain constant.[7] The fact that the plot obtained in the presence of hydrogen chloride crosses that obtained with stannic chloride alone is reasonably to be attributed to this cause.

Any free stannic chloride in solution, while it would increase indicator ionisation, would form a complex also with the anisole, and in so doing probably deactivate the ring, and so decrease the exchange rate. Thus, were any free stannic chloride actually present, the observed parallelisms between isotope exchange rate and indicator ionisation seem unlikely to exist. If straight lines were observed, they would have slopes less than unity. Further the ultraviolet absorption spectrum of anisole in the $SnCl_4$–$CH_3{\cdot}CO_2H$ system provides no evidence of complex formation. Altogether, therefore, it seems likely that little free stannic chloride is present in solutions in acetic acid (at any rate below 3M) and that indicator ionisation reflects only a Brønsted acidity.

EXPERIMENTAL

Materials.—Anhydrous acetic acid, m. p. >16·6°, was prepared as previously described.[6] The indicators were recrystallised samples. Baker "Analysed" stannic chloride was used for most experiments. Hydrogen chloride was that supplied in lecture bottles by Matheson Co. Inc. *p*-Deuteroanisole was a sample from previous work.[6] Ordinary anisole was redistilled, b. p. 154°.

Ionisation Measurements.—These were made by standard techniques[7] with a Beckman spectrophotometer at 23° ± 2°. All solutions except those of *p*-nitroaniline were reasonably stable. A small extrapolation to zero time was used for *p*-nitroaniline.

Ultraviolet Spectrum of Anisole.—Usanovich and Pichugina's experiments with mixtures of anisole and stannic chloride show that a dissociating complex is formed which is bright yellow.[12] Experiments with anisole in solutions of stannic chloride in dichloroacetic acid (in which free stannic chloride is present) also indicate a coloured complex. The ultraviolet spectrum of anisole in the present $SnCl_4$–$CH_3{\cdot}CO_2H$ systems reveals no absorption at wavelengths >3000 Å. There can thus be negligible complex formation.

Exchange Experiments.—These were measured under homogeneous conditions at 25° by methods analogous to those previously described.[6] Anisole was stable in the solutions used.

Reliability of the Measurements.—The similarity between the shapes of the ionisation curves in the presence and the absence of hydrogen chloride and the large effect of small quantities of this compound make it difficult to be sure that some of the acidity exhibited by the, supposedly hydrogen chloride-free, stannic chloride solutions is not, in fact, due to either a small amount of solvolysis or a trace of hydrogen chloride in the stannic chloride. However, the spectra were stable with time, the exchange rates provided good first-order plots, and the

[12] Usanovich and Pichugina, *Zhur. obshchei Khim.*, 1956, **26**, 2415.

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addition of small quantities of water reduced the observed acidity. All these facts argue against solvolysis. Further, a specimen of stannic chloride, vacuum-distilled at room temperature with the collection of a middle cut (a procedure which should have removed at least some of any dissolved hydrogen chloride) showed no decrease in acidity.

This work was carried out under the auspices of the U.S. Atomic Energy Commission during the tenure of a Research Associateship.

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795. *Bis*cyclo*pentadienylrhenium Hydride.*

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The preparation and properties of bis*cyclo*pentadienylrhenium hydride, $(C_5H_5)_2ReH$, are described. In contrast to other known metal-complex hydrides of transition metals the compound behaves as a base somewhat weaker than ammonia and with acids it forms the cation $[(C_5H_5)_2ReH_2]^+$. High-resolution nuclear magnetic resonance and infrared spectra of the compound and its salts are given.

FOR the metals of the first transitional series from titanium to nickel, inclusive, the *cyclo*pentadienyl compounds of the formula $(C_5H_5)_2M$ have now been characterized.[1] With the exception of the manganese compound, these have metal-to-ring bonds of the " sandwich bond " type as in ferrocene.[2] The manganese compound is unique in that it is ionic and must be regarded as a *cyclo*pentadienide;[3] this view has been recently confirmed by paramagnetic resonance absorption studies.[4] In view of the marked difference between the chemistry of manganese and of rhenium it seemed unlikely that a rhenium compound of similar type would exist and it was expected that bis*cyclo*pentadienylrhenium compounds of the type formed by molybdenum and tungsten[5] would be obtained. A bis*cyclo*pentadienylrhenium compound has been prepared, but of an unexpected and unusual type.

When the general method for the preparation of *cyclo*pentadienyl compounds was used, involving the reaction of the metal halide with sodium *cyclo*pentadienide in tetrahydrofuran solution,[3] direct vacuum-sublimation of the product from rhenium pentachloride at 120—200° gave a yellow crystalline substance. Elemental analysis and molecular-weight determinations suggested that this was the neutral compound $(C_5H_5)_2Re$; it was insoluble in and unaffected by water, soluble in light petroleum, and, unlike $(C_5H_5)_2Mn$, it did not react with ferrous chloride in tetrahydrofuran solution to give ferrocene. The infrared spectrum was also consistent with the formulation as a sandwich-bonded bis*cyclo*pentadienyl compound, and further, the compound dissolved in dilute mineral acids to give solutions which contained a cation. This cation formed insoluble precipitates with silicotungstic acid, sodium tetraphenylborate, and Reinecke's salt similar to those obtained with other bis*cyclo*pentadienyl-metal cations in aqueous solution.

Measurement of the magnetic susceptibility of the compound both as the solid and in solution in benzene showed, however, that it was diamagnetic. The only acceptable explanation of this fact was that the compound was not $(C_5H_5)_2Re$, which would be paramagnetic, but was a hydride, $(C_5H_5)_2ReH$.

Proof of the presence of a hydrogen atom bound directly to the metal was first obtained

[1] For references see Fischer and Wilkinson, *J. Inorg. Nuclear Chem.*, 1956, **2**, 149.
[2] For references to electronic structures see Liehr and Ballhausen, *Acta Chem. Scand.*, 1957, **11**, 207.
[3] Wilkinson, Birmingham, and Cotton, *J. Inorg. Nuclear Chem.*, 1956, **2**, 95.
[4] Voitländer and Schimitschek, *Z. Elektrochem.*, 1957, **61**, 941.
[5] Cotton and Wilkinson, *Z. Naturforsch.*, 1954, **9b**, 417.

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by high-resolution nuclear magnetic resonance studies, as was reported in a preliminary note.[6] The present evidence available for the formulation of the compound as $(C_5H_5)_2ReH$ and of the cation as $[(C_5H_5)_2ReH_2]^+$ is as follows.

Nuclear Magnetic Resonance Studies.—A typical spectrum of the compound in saturated solution in benzene or carbon disulphide shows two main peaks, the first at 45 ± 2 cycles per second (at 40 Mc./sec.) and the second at 733 ± 2 cycles per second, both on the high-field side relative to water at 21°. The relative areas of these two peaks are 10 : 1 respectively. The first resonance peak lies in the region where the protons of ferrocene and other π-*cyclo*pentadienyl derivatives show resonances,[7] and is obviously attributable to the protons of the two equivalent π-*cyclo*pentadienyl groups in $(C_5H_5)_2ReH$. The low-intensity absorption at the high field can be attributed only to a proton which is diamagnetically very well shielded. At the time of the first measurements on this compound, no other proton resonances with such an unusual displacement were known. Shortly afterwards it became known [8] that cobalt hydrocarbonyl $HCo(CO)_4$ showed a similar, although somewhat smaller, proton chemical shift. Since then, however, numerous other compounds in which a hydrogen atom is probably bound directly to a transition-metal atom have been examined, *e.g.*, $H_2Fe(CO)_4$,[9] $HM(CO)_3C_5H_5$ (M = Cr, Mo, W),[7] $HPtCl(PR_3)_2$,[10] $HMn(CO)_5$, $H_2Mo(C_5H_5)_2$, and $H_2W(C_5H_5)_2$,[11] and it can now be assumed that large chemical shifts, of the order 450—800 c./sec. at 40 Mc./sec., are characteristic of hydrogen atoms directly bound to a transition-metal atom.

Infrared Spectra.—The infrared spectrum of $(C_5H_5)_2ReH$ and the corresponding deuteride $(C_5H_5)_2ReD$ have been measured over the range 625—3400 cm.$^{-1}$ in carbon disulphide solution, in Nujol mulls and on single crystals, a microscope attachment being used. The data are presented in Table 1.

TABLE 1. *Infrared spectra of biscyclopentadienylrhenium hydrogen and deuterium compounds.*

Compound	C–H	Re–H	Re–D	*cyclo*Pentadienyl
$(C_5H_5)_2ReH$ in CS_2	3100w	2030w	—	1391s, 1341w, 1260vw, 1182w, 1096s, 1053w, 1004s, 990s, 892m, 885m, 809s, 785s
$(C_5H_5)_2ReH$ crystal	3073w	2037w, 2000w	—	—
$(C_5H_5)_2ReD$ crystal	3040	—	1458, 1432	
$[(C_5H_5)_2ReH_2]Cl$ in Nujol mull	~3100w	2330vw?, 2360vw?, 2070vw?, 2250vw?		1413s, 1365w, 1100s, 1010s, 800s

Whilst the spectrum is generally similar to that of ferrocene, a band at 2000 cm.$^{-1}$ in the solution spectrum of intensity comparable with that of the C–H stretching band does not occur in ferrocene. This band is not present in solution spectra of $(C_5H_5)_2ReD$. In the single-crystal and mull spectra of $(C_5H_5)_2ReH$, splitting of the peak at ~2000 cm.$^{-1}$ occurs, presumably owing to crystalline interactions; the deuteride shows similar bands but displaced to ~1460 cm.$^{-1}$. The allocation of the sharp band at 2000 cm.$^{-1}$ in the solution spectrum to an Re–H stretching mode is therefore certain. From the solid-state spectra $\nu_{Re-H}/\nu_{Re-D} = 1{\cdot}396$ and $1{\cdot}397$ for the two peaks, respectively. This very high frequency, which is in the same region as the stretching frequencies in gaseous diatomic transition-metal hydrides, indicates a very strong metal-to-hydrogen bond consistent with the high thermal stability of the rhenium compound.

Mass Spectra.—In the study of the mass spectra of neutral bis*cyclo*pentadienyl-metal compounds,[12] examination of the spectra from $(C_5H_5)_2ReH$ unequivocally showed the presence of the ion $C_{10}H_{11}Re^+$.

[6] Birmingham and Wilkinson, *J. Amer. Chem. Soc.*, 1955, **77**, 3421.
[7] Piper and Wilkinson, *J. Inorg. Nuclear Chem.*, 1956, **3**, 104.
[8] Friedel, Wender, Shufler, and Sternberg, *J. Amer. Chem. Soc.*, 1955, **77**, 3951.
[9] Cotton and Wilkinson, *Chem. and Ind.*, 1956, 1305.
[10] Chatt, Duncanson, and Shaw, *Proc. Chem. Soc.*, 1957, 343.
[11] Down, Green, and Wilkinson, unpublished work.
[12] Friedman, Irsa, and Wilkinson, *J. Amer. Chem. Soc.*, 1955, **77**, 3689.

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Chemical Properties of $(C_5H_5)_2ReH$.—Bis*cyclo*pentadienylrhenium hydride forms lemon-yellow acicular crystals, m. p. 161—162°, from benzene, ether, or light petroleum. The compound is thermally stable to at least 250° and sublimes readily in a vacuum above 80°. It is soluble in carbon disulphide and hydrocarbon solvents, giving yellow solutions. In carbon tetrachloride the compound decomposes rather rapidly to give insoluble material which does not give a test for bis*cyclo*pentadienyl cations on dissolution in acids, together with chloroform; the formation of chloroform from carbon tetrachloride appears to be a characteristic reaction of compounds with transition-metal–hydrogen bonds (cf. ref. 7).

Whilst the solid compound reacts only slowly with air, and is decomposed, it may be handled for periods of a few minutes in air, but solutions of the compound are rapidly attacked, purple-brown decomposition products being obtained. The compound is insoluble in liquid ammonia, and no colour change occurs, unlike the cases of $(C_5H_5)_2V$ and $(C_5H_5)_2Cr$, which form ammoniates.[3]

The compound does not react with diazomethane in cold or refluxing ether, or with nitric oxide or carbon dioxide at ordinary pressures. Carbon monoxide at 100°/200 atm. converts it [13] into a compound of stoicheiometry $C_{10}H_{11}Re(CO)_2$, the structure of which we will discuss in a later paper. Although the hydride is unaffected by concentrated (8N) sodium hydroxide, it dissolves without effervescence in dilute hydrochloric or sulphuric acid. The solid hydride rapidly absorbs gaseous hydrogen chloride or bromide, and salts are formed quantitatively as white amorphous powders:

$$(C_5H_5)_2ReH + HCl \longrightarrow [(C_5H_5)_2ReH_2]Cl$$

It is interesting that the white solid in presence of excess of hydrogen chloride has a strong pink colour, which disappears on removal of the excess of gas; the pink colour may be due to the presence of an easily dissociated salt $[(C_5H_5)_2ReH_2]^+HCl_2^-$ similar to those formed by cæsium and other large cations.[14]

These salts are exceedingly deliquescent and must be handled in a vacuum or in an inert dry atmosphere. The colourless aqueous solutions give the usual precipitation reactions characteristic of bis*cyclo*pentadienyl-metal cations; the reineckate has been analysed. The solutions are fairly rapidly decomposed by air, and oxidation by chemical agents completely disrupts the cation.

Addition of ammonia or alkali to the aqueous solutions liberates the free base $(C_5H_5)_2ReH$, which can be quantitatively recovered by solvent extraction:

$$[(C_5H_5)_2ReH_2]^+ + OH^- \longrightarrow (C_5H_5)_2ReH + H_2O$$

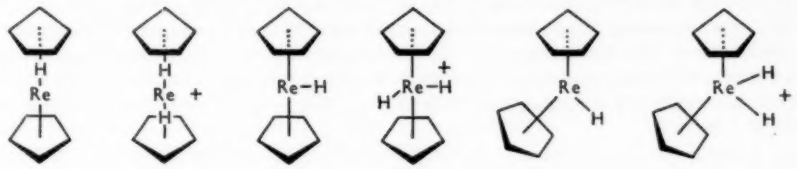
The $(C_5H_5)_2ReH$–$[(C_5H_5)_2ReH_2]^+$ system is thus analogous to the NH_3–NH_4^+ system, except that the base is insoluble in water. Determining the base constant by pH measurement and titrations of $(C_5H_5)_2ReH$ at 25° with acid and of $[(C_5H_5)_2ReH_2]Cl$ with base, in 60% dioxan solution, gave a value of pK 8·5. The value for ammonia in 60% dioxan interpolated from published data [15] is pK 8·85.

The nuclear magnetic resonance spectrum of the cation, which is discussed below, confirms the stoicheiometry $[(C_5H_5)_2ReH_2]^+$.

Discussion.—The bis*cyclo*pentadienylrhenium hydride is the only bis*cyclo*pentadienylrhenium compound that we have been able to isolate. Attempts to obtain species that might have been expected to exist, such as $(C_5H_5)_2ReCl_n$, failed. No products of this type were obtained either by reaction of stoicheiometric amounts of rhenium pentachloride with *cyclo*pentadiene in piperidine and diethylamine [3] or with sodium *cyclo*pentadienide. In the former reaction extractions of the dry product even with aqueous acid gave no evidence for bis*cyclo*pentadienyl-metal ions; and in the latter only the hydride could be extracted with light petroleum or chloroform or the $[(C_5H_5)_2ReH_2]^+$ ion with dilute acid.

[13] Fischer and Wirtzmuller, *Z. Naturforsch.*, 1957, **12b**, 737.
[14] See, *e.g.*, West, *J. Amer. Chem. Soc.*, 1957, **79**, 4568; Waddington, *J.*, 1958, 1708; Sharp, *J.*, 1958, 2558.
[15] Rumpf, Gerault-Vexlearschi, and Schoal, *Bull. Soc. chim. France*, 1955, 554.

There are several possible structures for the hydride and its cation. Liehr [16] has suggested that the hydrogen atom in the hydride and two hydrogen atoms in the cation can be located between the *cyclo*pentadienyl rings and the metal atom (IA, IB). The hydrogen atoms are considered to be in the $d(a_{1g})$ orbital, which, according to a molecular-orbital view of the bonding in neutral bis*cyclo*pentadienyl-metal compounds, is non-bonding as far as the primary metal–ring bonding is concerned. Of other possible structures for the hydride, (IIA) and (IIC) are the most likely; in (IIA), the *cyclo*pentadienyl rings are



(IA) (IB) (IIA) (IIB) (IIC) (IID)

aligned as in ferrocene, in (IIC) the metal–ring axes are at an angle. Corresponding structures for the cation are (IIB and D, respectively). Either of the structures (I, II) could equally well account for the large chemical shift of the hydridic hydrogen atom and for the basic character of the hydride.

The infrared spectrum of the cation $[(C_5H_5)_2ReH_2]^+$ might have been expected to provide useful information, since, if the hydrogen atoms were symmetrically located between the rings (IB) or symmetrically on either side of the metal atom (IIB), only one Re–H stretching frequency would be expected. For structures with the hydrogen atoms at an angle (IIB, IID), both symmetric and asymmetric vibrations should be observed. Unfortunately, however, the Re–H stretching bands are so weak that even by using very concentrated aqueous solutions of the salt we have been unable to identify the Re–H bands reliably. In the solid-state spectra of the hydride, the Re–H bands are split. The solid-state splitting of the hydride is rather difficult to reconcile with formula (IA), since with the hydrogen atoms buried between the metal atoms and the ring it is not easy to see how intermolecular interaction in the crystal lattice could affect such hydrogen atoms.

TABLE 2. *Nuclear magnetic resonance data at* 40 *Mc./sec.*

The high field side is designated −; shifts are referred to water at 21° ± 1·0°.

Compound	Proton resonance (cycles)	Relative intensity	Assignment	Fine structure	Multiplet width (cycles)	Splitting (cycles)
$(C_5H_5)_2ReH$ in C_6H_6 and CS_2	−46	10	π-C_5H_5	Doublet	1·9	$1·0_5$
	−732	1	hydridic	Not detected	18	
$(C_5H_5)_2ReD$ in C_6H_6	−46	—	π-C_5H_5	Singlet	$\leqslant$0·5	—
	No hydride peak	—	—			
$[(C_5H_5)_2ReH_2]^+Cl^-$ in H_2O	+33	10	π-C_5H_5	Triplet	1·45	0·56 *
	−734·5	2	hydridic	Not detected	$\approx$8	
$[(C_5H_5)_2ReD_2]^+Cl^-$ in D_2O	+32·5	—	π-C_5H_5	Singlet	$\leqslant$0·5	—
	No hydride peak	—	—			

* Confirmed also by the ringing-beat procedure (Reilly, *J. Chem. Phys.*, 1956, **25**, 604).

The nuclear magnetic resonance data are presented in Table 2. Whilst all four compounds show the resonances due to the *cyclo*pentadienyl ring hydrogen atoms, and the hydrides show the shielded-proton resonances, the fine structure on these resonances is more consistent with structure (II) than with Liehr's model, and we consider first the consequences of (II). The absence of fine structure on the *cyclo*pentadienyl peaks in the deuterides, and its appearance in the hydrides, suggests that this structure is produced by

[16] Liehr, *Naturwiss.*, 1957, **44**, 61.

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the indirect spin–spin coupling interaction [17] between the hydridic proton(s) and the ring protons, and is not attributable to chemical shifts of non-equivalent *cyclo*pentadienyl rings. The single proton in $(C_5H_5)_2ReH$ should split the *cyclo*pentadienyl peak into a symmetrical doublet, and two equivalent protons in $[(C_5H_5)_2ReH_2]^+$ should split the *cyclo*pentadienyl peak into a triplet with intensity ratios 1 : 2 : 1. The replacement of hydrogen by deuterium which has spin 1 would be expected to split the *cyclo*pentadienyl peak into a triplet in $(C_5H_5)_2ReD$ and a quintuplet in $[(C_5H_5)_2ReD_2]^+$, but the smaller magnetic moment of the deuteron (about one-third of that of the proton) would mean that these splittings would be only about one-third as great, so that they would not be resolved under the conditions of the measurements. It is also possible that these splittings would be removed by quadrupole relaxation [18] of the deuterium nucleus. In fact, a single peak is observed of width 0·5 cycle/sec. in both deutero-compounds, any fine structure being obscured.

The hydridic-proton peaks in both hydride compounds should also show a splitting by the ten *cyclo*pentadienyl ring protons into eleven components, the splitting being $1{\cdot}0_5$ cycles/sec. in $(C_5H_5)_2ReH$ and 0·56 cycle/sec. in the cation. Although the overall line-width of the hydride peak of the cation is about twice that in the neutral compound, no splitting was observed on these peaks: this is not surprising, since both were weak and could not be measured under conditions required for good resolution. No splitting of either the hydridic- or the *cyclo*pentadienyl-proton peaks was found which could be attributed to spin–spin coupling of the protons with the magnetic moments of the two rhenium nuclei, but this splitting would probably be destroyed since both these nuclei have large electric quadrupole moments.[18]

As noted above, the observed data are consistent with formulation (II). Now in structure (IA) the two *cyclo*pentadienyl rings are not equivalent in that a proton is inserted between one of them and the metal atom, and they would be expected to give rise to a double peak in both $(C_5H_5)_2ReH$ and $(C_2H_5)_2ReD$; also in the former each of these two peaks would be split by unequal amounts by the hydridic proton. For the cations, $[(C_5H_5)_2ReD_2]^+$ should give one peak, but the *cyclo*pentadienyl peaks in $[(C_5H_5)_2ReH_2]^+$ would be split into a doublet by the nearest proton and each further split into a doublet by the more distant proton, although the ratios of these two doublet splittings could conceivably overlap to give the appearance of the triplet.

The nuclear magnetic resonance data do not allow a distinction to be made between the two main structural types (IIA,B) and (IIC,D). There is nothing in the spectra of the hydride or the deuteride to indicate that the *cyclo*pentadienyl rings are not freely rotating in the free molecule, and such free rotation is known to occur for ferrocene and some of its substitution products. The relative dispositions of the rings shown in (IIA—D) are merely symbolic. The large displacement (79 cycles/sec.) of the *cyclo*pentadienyl peaks to lower applied fields in the cations relatively to the neutral molecules may be significant, but the present state of knowledge on chemical shifts in *cyclo*pentadienyl-metal compounds is not yet adequate to provide an explanation.

It is to be noted that the protons in the cation undergo only very slow exchange with protons in aqueous solution. In aqueous solutions which are slightly acid, the appearance of the hydridic peak shows [19] that the average chemical lifetime of the proton on the cation must be $>1/(2\pi \times 730)$ sec.$^{-1}$. If, as discussed above, the triplet on the *cyclo*pentadienyl-proton resonance is attributed to splitting by the hydridic protons, then the minimum lifetime must be even greater than this or of the order of $1/(2\pi \times 0{\cdot}56)$, *i.e.*, 0·3 sec. It may be also noted that in one preparation of $(C_5H_5)_2ReD$, the $[(C_5H_5)_2ReH_2]Cl$ salt was dissolved in a large excess of D_2O and after 20 min. NaOD in D_2O was added: the resulting neutral product showed a pronounced hydridic-proton resonance. After equilibration

[17] Gutowsky, McCall, and Slichter, *J. Chem. Phys.*, 1953, **21**, 279.
[18] Pople, *Mol. Phys.*, 1958, **1**, 168.
[19] Gutowsky and Saika, *J. Chem. Phys.*, 1953, **21**, 1688.

of the hydrogen chloride salt for 12 hr. under the same conditions, the recovered product had no detectable hydridic-proton resonance.

Experimental

Preparations and operations with the rhenium compounds were carried out in oxygen-free nitrogen in a glove-box or in a vacuum. Solvents and reagent solutions were thoroughly degassed before use. Infrared spectra were measured with a Perkin-Elmer Model 21 spectrophotometer with both sodium chloride and calcium fluoride optics. Single-crystal measurements were made with the assistance of Dr. Orr at the Chester Beatty Research Institute, using a microscope attachment to a single-beam Perkin-Elmer instrument. High-resolution nuclear magnetic resonance spectra were measured at 40 Mc./sec. on a Varian Associates Model 4300 B spectrometer with super-stabiliser. Microanalyses of $(C_5H_5)_2ReH$ were obtained through the courtesy of Dr. E. O. Brimm of Linde Air Products, Tonawanda, N.Y.; other analyses were by the Microanalytical Laboratory, Imperial College.

*Bis*cyclo*pentadienylrhenium Hydride.*—Rhenium pentachloride was prepared by direct chlorination of the metal at 600°; the product was sublimed in nitrogen to remove oxychlorides. To a cold solution (0°) of sodium *cyclo*pentadienide (0·2 mole) in tetrahydrofuran (150 ml.) was added solid rhenium pentachloride (0·03 mole). The purple mixture was stirred for ~5 hr. with heating to 50°. Originally the solvent was removed at this point and the hydride was sublimed in a vacuum from the residue at 120—200°. The product always contained some oil and subsequent purification was difficult; the light petroleum solution was extracted with 2N-hydrochloric acid and after washing of the aqueous layer with light petroleum the hydride was liberated by alkali and extracted into light petroleum. It was then crystallized from light petroleum and sublimed in a vacuum. These steps were repeated several times. A better procedure, which gives a purer product and higher yields, is to add sodium borohydride (0·08 mole) to the reaction mixture in tetrahydrofuran; after a further hour's refluxing, the solvent was removed and the product sublimed as pale yellow crystals free from oil and sticky material in yields of 35—40% based on $ReCl_5$. This product was purified by crystallisation from light petroleum and by sublimation. The molecular weight was determined by Clark's modification of the Signer isothermal method,[20] ether and benzene being used as solvents and ferrocene as a reference. From two measurements in each solvent, $M = 310 \pm 5$ [Calc. for $(C_5H_5)_2ReH$: M, 317·5].

The magnetic susceptibility was measured on the solid and the melt over the range 77—510° K, by the Gouy method. $\chi_{mol}^{373} = -135 \pm 5 \times 10^{-6}$ c.g.s. unit. The compound was also diamagnetic in benzene solution (16 mg./ml.).

*Bis*cyclo*pentadienylrhenium Deuteride.*—The sublimed hydride (~0·5 g.) was dissolved in 2N-deuterium chloride in D_2O (~10 ml.); the base was liberated by addition of 6N-sodium deuteroxide in D_2O and was extracted with light petroleum. The procedure was then repeated; the deuteride, finally purified by sublimation, had m. p. 168—169°. The yield was ~90%.

*Bis*cyclo*pentadienylrhenium Dihydrogen Chloride* (*Bromide*).—The hydride was treated with hydrogen chloride at room temperature. A rapid reaction gave the *chloride* as a white powder, from which excess of the gas was removed by pumping {Found: Re, 52·0; Cl, 8·5. $[(C_5H_5)_2ReH_2]Cl$ requires Re, 52·65; Cl, 8·6%}. The compound sublimes slightly at ~140° in a vacuum with extensive decomposition; no hydride is formed.

A bromide was similarly obtained.

Addition of Reinecke's salt to aqueous solutions of the salt gives a rose pink precipitate of the *derivative* {Found: C, 26·1; H, 2·4; Re, 29·5; Cr, 8·2. $[(C_5H_5)_2ReH_2][Cr(NH_3)_2(CNS)_4]$ requires C, 26·5; H, 2·5; Re, 29·4; Cr, 8·2%}.

Physical Measurements.—Nuclear magnetic resonance measurements on the hydride were made by using both benzene and carbon disulphide saturated solutions with a water capillary reference; the cation was studied in concentrated aqueous solution with a *cyclo*hexane capillary reference. The measurements were made at 21° ± 1·0°. The solutions were contained in spinning 5 mm. (outer diameter) sealed Pyrex tubes, with sealed capillary internal reference tubes. The base constant of the hydride was determined in 60% dioxan solution by titration

[20] Weissberger (Editor), "Technique of Organic Chemistry," Interscience Publ. Inc., New York, 1954, Vol. VI.

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with standard acid; the titration curve was repeated by titrating the chloride with standard base. The pH of the solutions was measured with a Cambridge Instrument Co. pH meter and a glass electrode. The neutralisation curves were typical of those for a weak base. The pH of the hydride in the dioxan solution (0·0224 mole/l.) was 10·13.

We are indebted to the European Research Associates for financial support (to M. L. H. G.), and to Johnson, Matthey and Co. Ltd. for the loan of rhenium metal. Part of this work was done in the Mallinckrodt Laboratory, Harvard University, and thanks are offered to Dr. J. M. Birmingham for his assistance. The senior author is indebted to the John Simon Guggenheim Foundation for a Fellowship, and to Professor J. Bjerrum for the hospitality in his laboratories.

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796. *Preparation of Unsaturated Keto-acids from the Interaction of Ethylene and Acid Anhydrides.*

By H. T. TAYLOR.

Ethylene and acid anhydride–aluminium chloride complexes in ethylene chloride provide unsaturated keto-acids in low yield. With maleic anhydride 6-methyl-4-oxohepta-2 : 5-dien-1-oic acid is unexpectedly obtained. By using the corresponding half ester chlorides higher yields are obtained.

THE reaction of ethylene and *cyclo*hexene with acid chloride–aluminium chloride complex in methylene or ethylene chloride has been reported.[1] This paper is concerned with the application of these solvents to the Friedel–Crafts acylation of ethylene with succinic and maleic anhydride and related compounds. Experimental procedure was complicated, partly by the low solubility of the anhydrides and their complexes and partly by polymerisation, and products were obtained in only poor yield. Higher yields were obtained by replacing the acid anhydride with the corresponding half ester chloride.

Ethylene and succinic anhydride reacted at a convenient rate at 25—30°, and reaction was essentially complete when 1 mol. of ethylene had been absorbed. The main product was 4-oxohex-5-enoic acid. Catalytic hydrogenation converted this acid into 4-oxohexanoic acid, which was identified as its oxime and semicarbazone.

$$CH_2{:}CH_2 + \overbrace{CO{\cdot}CH_2{\cdot}CH_2{\cdot}COO} \longrightarrow CH_2{:}CH{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$$

Ethylene and maleic anhydride reacted at 25°, but only in the presence of excess of aluminium chloride, and more than 2 mols. of ethylene were absorbed before reaction slackened. Decomposition of the mixture with hydrochloric acid and ice, esterification with diazomethane, and distillation under reduced pressure from anhydrous sodium carbonate gave a product from which methyl 6-methyl-4-oxohepta-2 : 5-dienoate was isolated.

$$2CH_2{:}CH_2 + \overbrace{CO{\cdot}CH{:}CH{\cdot}COO} \longrightarrow Me_2C{:}CH{\cdot}CO{\cdot}CH{:}CH{\cdot}CO_2H$$

Recently, Matsumoto, Hata, and Nischida [2] observed a similar reaction, acylation of ethylene with benzoyl chloride in tetrachloroethane in the presence of excess of aluminium chloride giving *iso*butenyl phenyl ketone. In absence of an excess of aluminium chloride, the expected product, phenyl vinyl ketone, was obtained. These authors carried out the reaction at 0° during 24 hr. and obtained *iso*butenyl phenyl ketone in 30—50% yield:

$$2CH_2{:}CH_2 + Ph{\cdot}CO{\cdot}Cl \longrightarrow Ph{\cdot}CO{\cdot}CH{:}CMe_2$$

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[1] Baddeley, Taylor, and Pickles, *J.*, 1953, 124.
[2] Matsumoto, Hata, and Nischida, *J. Org. Chem.*, 1958, **23**, 106.

In ethylene dichloride, ethylene was found to react readily with benzoyl chloride–aluminium chloride complex in the presence of excess of aluminium chloride at 25°, and a 40% yield of *iso*butenyl phenyl ketone was obtained in 1 hr.

The low yields obtained by using the anhydride–aluminium chloride complex suggested the use of the corresponding half ester chloride; the problem of limited solubility of the acid anhydride and its complex with aluminium chloride is then overcome. Reaction of ethylene with β-methoxycarbonylpropionyl chloride and with γ-methoxycarbonylbutyryl chloride, using 1 mol. of aluminium chloride, occurred readily at 35°, ceased sharply when 1 mol. of ethylene had been absorbed, and afforded methyl 4-oxohex-5-enoate and 5-oxohept-6-enoate, respectively, in good yield. Distillation under reduced pressure from anhydrous sodium carbonate is necessary to remove traces of chlorine. In contrast, there was no reaction between ethylene and β-methoxycarbonylacryloyl chloride.

Interaction of ethylene with acylating agents.

Acylating agent	Temp.	Product	Yield (%)
$(Me\cdot CO)_2O$ [1]	−5°	$Me\cdot CO\cdot CH_2\cdot CH_2Cl$	40
$CO\cdot CH_2\cdot CH_2\cdot CO$	30	$CH_2{:}CH\cdot CO\cdot CH_2\cdot CH_2\cdot CO_2H$	25
Poly(adipic anhydride)	20—60	—	0
$CO\cdot CH{:}CH\cdot CO$	25	$Me_2C{:}CH\cdot CO\cdot CH{:}CH\cdot CO_2H$	15
$MeO_2C\cdot[CH_2]_2\cdot COCl$	35	$CH_2{:}CH\cdot CO\cdot[CH_2]_2\cdot CO_2Me$	85
$MeO_2C\cdot[CH_2]_2\cdot COCl$	35	$CH_2{:}CH{:}CO\cdot[CH_2]_2\cdot CO_2Me$	40
$MeO_2C\cdot CH{:}CH\cdot COCl$	30—60	—	0
$Ph\cdot COCl$	30	$Ph\cdot CO\cdot CH{:}CMe_2$	40

The saturated keto-acids required for identification were obtained in 40—50% yield from the corresponding dialkylcadmium and the appropriate half ester chloride, following Gilman and Nelson's method.[3] The use of the Grignard compound $R\cdot MgBr$ [4] was unsuccessful when applied to R = alkyl, and the alkylzinc halides [5] gave poor yields.

Experimental

Ethylene and Succinic Anhydride.—Powdered aluminium chloride (0·60 mole) was added with stirring to succinic anhydride (0·25 mole) in ethylene dichloride (500 ml.). The succinic anhydride–aluminium chloride complex solution was decanted from excess of aluminium chloride, and dry ethylene passed into the agitated solution at 25°; absorption ceased when 12 l. had been absorbed. The product was poured into dilute hydrochloric acid and ice, and the dried (Na_2SO_4) organic layer distilled under reduced pressure in the presence of anhydrous sodium carbonate giving 4-oxohex-5-enoic acid (7 g.), b. p. 146—148° (Found: C, 55·9; H, 6·2. Calc. for $C_6H_8O_3$: C, 56·2; H, 6·3%). A sample (2·00 g.) in ethanol (25 ml.) absorbed hydrogen (353 ml.; corr. to S.T.P. Required 350 ml.) in the presence of palladium (0·2 g.). The reduced product, b. p. 151°/10 mm., readily afforded an oxime, m. p. 72°, and a semicarbazone, m. p. 168°, which did not depress the m. p.s of the corresponding derivatives of 4-oxohexanoic acid.

Ethylene and Maleic Anhydride.—Powdered aluminium chloride (1·2 moles) was added to maleic anhydride (0·50 mole) in ethylene dichloride (400 ml.). Dry ethylene was passed into the agitated solution maintained at <30°. After 30 l. had been absorbed, the mixture was poured into dilute hydrochloric acid and ice, and the organic layer dried (Na_2SO_4). Removal of the solvent gave a dark residue (36 g.). This was set aside with ethereal diazomethane [prepared from methylnitrosourea (30 g.)] for 1 hr., the ether was removed, and the residue was distilled under reduced pressure, affording a main fraction (17 g.), b. p. 95°/0·2 mm. The yellow solid, obtained by cooling at 0°, was recrystallised from light petroleum (b. p. 0—40°), giving methyl 6-methyl-4-oxohepta-2 : 5-dienoate (11 g.), m. p. 40° (Found: C, 63·9; H, 7·1. Calc. for $C_9H_{12}O_3$: C, 64·2; H, 7·1%). A Kuhn–Roth estimation of terminal methyl group gave 8·1% *C*-Me. (Calc. for 1 *C*-Me 8·9%). Ozonolysis of the product, followed by decomposition of the ozonide with 2N-sodium hydroxide, afforded acetone (2 : 4-dinitrophenylhydrazone,

[3] Gilman and Nelson, *Rec. Trav. chim.*, 1936, **55**, 518.
[4] Fieser and Dandt, *J. Amer. Chem. Soc.*, 1941, **63**, 782.
[5] Clutterbuck and Raper, *J. Biochem.*, 1925, **19**, 390.

m. p. 128°). A sample (5·00 g.) in ethanol (40 ml.) absorbed hydrogen (1310 ml., corr. to S.T.P. Calc. for $C_9H_{12}O_3$: 1333 ml.) in the presence of palladium (0·2 g.). The reduced product was hydrolysed by dilute hydrochloric acid. The acid, b. p. 112°/10 mm., readily formed a semicarbazone, m. p. 148°, which did not depress the m. p. of the semicarbazone of 6-methyl-4-oxoheptanoic acid, m. p. 148°, but did depress that of the semicarbazone of 4-oxo-octanoic acid, m. p. 155°.

Ethylene and Poly(adipic Anhydride).—Dry ethylene did not react with the poly(adipic anhydride)–aluminium chloride complex in ethylene dichloride. The addition of more aluminium chloride also had no effect.

Ethylene and β-Methoxycarbonylpropionyl Chloride.—β-Methoxycarbonylpropionyl chloride (0·25 mole) was added to a suspension of aluminium chloride (0·30 mole) in ethylene dichloride (200 ml.). The complex was decanted from excess of aluminium chloride. Dry ethylene was absorbed at a steady rate at 35° until 6 l. had been taken up. The product was then poured into dilute hydrochloric acid and ice, and the dried (Na_2SO_4) organic layer distilled twice under reduced pressure from anhydrous sodium carbonate, giving methyl 4-oxohex-5-enoate (27 g.), b. p. 96°/10 mm. (Found: C, 59·0; H, 6·9. Calc. for $C_7H_{10}O_3$: C, 59·2; H, 7·0%). The ester (5·00 g.) in ethanol (40 ml.) absorbed hydrogen (794 ml., corr. to S.T.P. Calc. for $C_7H_{10}O_3$: 788 ml.) in the presence of palladium (0·2 g.) giving methyl 4-oxohexanoate, b. p. 92°/10 mm., identified as its semicarbazone, m. p. 142°.

Ethylene and γ-Methoxycarbonylbutyryl Chloride.—γ-Methoxycarbonyl butyryl chloride (0·25 mole) was treated exactly as was β-methoxycarbonylpropionyl chloride (0·25 mole), providing methyl 5-oxohept-6-enoate (15 g.), b. p. 110°/12 mm. (Found: C, 61·3; H, 7·7. Calc. for $C_8H_{12}O_3$: C, 61·5; H, 7·7%). The product was hydrogenated to methyl 5-oxoheptanoate, identified as its semicarbazone, m. p. 106°.

Ethylene and Benzoyl Chloride.—Dry ethylene was passed into an agitated solution of benzoyl chloride (0·25 mole) and aluminium chloride (0·35 mole) in ethylene chloride (200 ml.), and the temperature kept below 30° by cooling. After 30 l. of ethylene had been absorbed the mixture was poured into dilute hydrochloric acid and ice. The organic layer was dried (Na_2SO_4) and distilled giving *iso*butenyl phenyl ketone (17 g.), b. p. 122—124°/10 mm. The product gave a 2 : 4-dinitrophenylhydrazone, m. p. 180—181° (Matsumoto, Hata, and Nischida [2] record m. p. 180—181°).

β-*Methoxycarbonylpropionyl Chloride.*—Succinic anhydride (1 mole) was gently refluxed with methanol (1 mole) for 30 min.; the thionyl chloride (1·2 moles) was added and the mixture refluxed for 1 hr. The excess of thionyl chloride was distilled off and the residue distilled giving β-methoxycarbonylpropionyl chloride (0·90 mole), b. p. 87°/14 mm.

γ-*Methoxycarbonylbutyryl Chloride.*—This was similarly prepared from glutaric anhydride. It had b. p. 98°/12 mm.

β-*Methoxycarbonylacryloyl Chloride.*—Fumaric acid (1 mole) was ground with phosphorus pentachloride (2 moles) and the mixture heated (water-bath) for 3 hr. The product was distilled, giving, after removal of phosphorus oxychloride, fumaroyl dichloride (0·63 mole), b. p. 62°/12 mm. Methanol (0·63 mole) was added, the mixture refluxed for 1 hr., and the product distilled. β-Methoxycarbonylacryloyl chloride (0·58 mole), b. p. 83°/12 mm., was obtained.

Saturated Keto-acids.—Powdered cadmium bromide (0·1 mole) was added to the alkylmagnesium halide (0·2 mole) in sodium-dried ether (150 ml.), and the mixture was refluxed for 3 hr. The required half ester chloride (0·2 mole) was then added and the mixture refluxed for a further 3 hr., with stirring until the product solidified. Dilute sulphuric acid was added and the organic layer was dried (Na_2SO_4). Removal of the solvent and distillation under reduced pressure afforded the methyl ester of the required keto-acid (see Table).

Keto-acid	B. p.	Ester, b. p.	Semicarbazone of acid, m. p.	Semicarbazone of ester, m. p.
$EtCO{\cdot}[CH_2]_2{\cdot}CO_2H$	142°/10 mm.	91°/14 mm.	186°	142°
$PrCO{\cdot}[CH_2]_2{\cdot}CO_2H$	—	102°/10 mm.	—	106°
$BuCO{\cdot}[CH_2]_2{\cdot}CO_2H$	155°/10 mm.	112°/10 mm.	155°	—
$Bu^tCO{\cdot}[CH_2]_2{\cdot}CO_2H$	155°/10 mm.	112°/10 mm.	148°	102°
$EtCO{\cdot}[CH_2]_3{\cdot}CO_2H$	—	104°/10 mm.	—	106°

The author thanks Dr. G. Baddeley for his interest.

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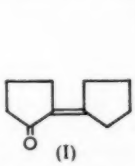
797. *High-temperature* (300—350°) *Reactions of* cyclo*Pentanone and Some of its Derivatives with Ammonia and Aliphatic Amines.*

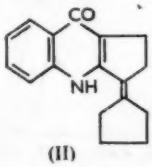
By O. B. Edgar and David H. Johnson.

The products obtained when *cyclo*pentanone is heated at 300° under autogenous pressure with anhydrous ammonia or with aliphatic amines have been found to be complex mixtures in which alkylated *cyclo*pentanones and pyridine bases, *e.g.*, 6-alkyl-2 : 3-4 : 5- or 4-alkyl-2 : 3-5 : 6-di*cyclo*penteno-pyridines, predominate. Similar products arise in the vapour phase at 350° under base-catalysis.

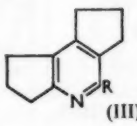
The studies now reported form part of a comprehensive investigation undertaken in 1952—1956 into the mode of thermal decomposition of Nylon 66 polymer.[1,2]

Although the condensation of saturated and αβ-unsaturated aldehydes and ketones with ammonia and its derivatives, which leads to substituted pyridines, is one of the oldest of synthetical procedures,[3,4] studied particularly by Tschitschibabin and his associates,[5] little information has been available concerning the reactions of cyclic ketones with such bases. Blount and Plant [6] have shown that, unlike *cyclo*hexanone, suberone, and perhydroindan-1-one which behave normally in the Tiedtke condensation [7] with anthranilic acid, *cyclo*pentanone, the ketone which is of special interest in matters relating to the thermal stability of Nylon 66 polymer, undergoes self-condensation to 2-*cyclo*pentylidene-*cyclo*pentanone (I) before ring-closure to the quinolone (II). From the products of reaction of *cyclo*pentanone with acetaldehyde and ammonia, Tschitschibabin [8] isolated 6-methyl-

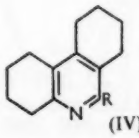

(I)



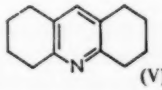
(II)



(III)



(IV)



(V)

2 : 3-4 : 5-di*cyclo*pentenopyridine (III; R = Me); he also studied the reactions between *cyclo*hexanone and aldehydes and ammonia and showed,[9] for example, that *cyclo*hexanone, formaldehyde, and ammonia yield a mixture containing the octahydrophenanthridine (IV; R = H) and octahydroacridine (V), with the former predominant. Patent literature [10] contemporaneous with the present investigation describes the production of polycyclic bases from the condensation of anhydrous ammonia with *cyclo*pentanone and *cyclo*hexanone severally, under autogenous pressure at temperatures below 200°. The constants quoted for these substances, which appear to be of indefinite structure and are claimed to possess certain fungicidal and insecticidal activity, show considerable differences from those of our materials isolated from reactions at higher temperatures (300—350°).

We found that when *cyclo*pentanone was heated at 300° under autogenous pressure with 1·2 mol. of anhydrous ammonia, the volatile neutral products (5—6% by wt.) contained 2-*cyclo*pentylidene*cyclo*pentanone (I), 2-*cyclo*pentyl*cyclo*pentanone (VI), and a trace of a crystalline amide, possibly δ-*cyclo*pent-1-enylvaleramide (VII; R = NH_2).

[1] Goodman, *J. Polymer Sci.*, 1954, **13**, 175.
[2] *Idem*, *ibid.*, 1955, **17**, 587; Ph.D. Thesis, London, 1957.
[3] Hübner and Geuther, *Annalen*, 1860, **114**, 35.
[4] Baeyer, *Ber.*, 1869, **2**, 398; *Annalen*, 1870, **155**, 281, 294.
[5] For collected references see Tschitschibabin, "Traité de Chimie Organique," Masson, Paris, 1953, Vol. XX, p. 57.
[6] Blount and Plant, *J.*, 1937, 376.
[7] Tiedtke, *Ber.*, 1909, **42**, 621.
[8] Tschitschibabin, *Bull. Soc. chim. France*, 1939, **6**, 522.
[9] Tschitschibabin and Barkovsky, *Compt. rend.*, 1941, **212**, 914.
[10] U.S.P. 2,692,268/1954; 2,693,491/1954.

The major component of the basic products (22—23% by wt.) was a liquid tertiary base $C_{15}H_{21}N$ containing no active hydrogen and giving a crystalline chloroplatinate but no other satisfactory derivatives. The ultraviolet absorption (Fig. 1) was consistent with the presence of a vinylic amine system,[11] *e.g.*, as in pyridine bases,[12] and, in particular, was closely similar to that of the pyridine derivative (III; R = Pr^n) described by Goodman.[2] The infrared spectrum of our base $C_{15}H_{21}N$ and of Goodman's compound were also similar, *e.g.*, bands at 1605 and 1585 cm.$^{-1}$ indicating a heterocyclic nucleus, whereas absence of bands in the 3500—3300 and the 3100—3000 cm.$^{-1}$ region indicated absence of $-NH-$ and aromatic C–H groups. Further, the mass-spectral breakdown pattern of the two bases was analogous. Thus the spectral characteristics suggest that our base $C_{15}H_{21}N$ is 6-*n*-butyl-2 : 3-4 : 5-di*cyclo*pentenopyridine (III; R = Bu^n), and in keeping with this its chemical properties paralleled closely those of the lower homologue (III; R = Pr^n). When

FIG. 1. FIG. 2.

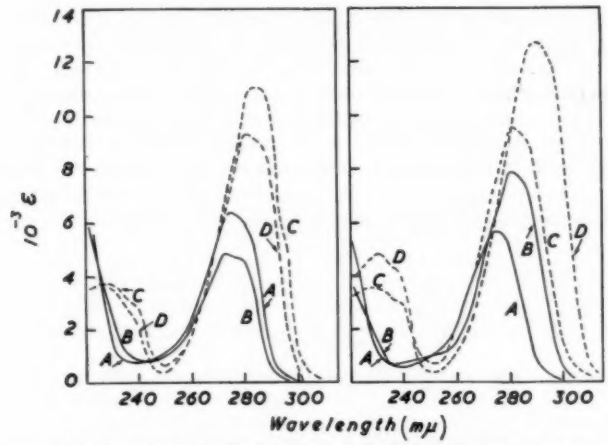
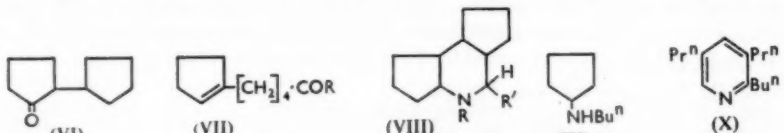


FIG. 1. 6-n-*Butyl*-2 : 3-4 : 5-di*cyclopentenopyridine* (*A*) *in* MeOH, (*C*) *in conc.* HCl.
1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*Octahydro*-9-n-*pentylphenanthridine* (*B*) *in* MeOH, (*D*) *in conc.* HCl.

FIG. 2. 2-n-*Propyl*-3 : 4-5 : 6-di*cyclopentenopyridine* (*A*) *in* MeOH, (*C*) *in conc.* HCl.
4-n-*Propyl*-2 : 3-5 : 6-di*cyclopentenopyridine* (*B*) *in* MeOH, (*D*) *in conc.* HCl.

freshly isolated, our base (III; R = Bu^n) gave a red colour with alcoholic 1 : 3 : 5-trinitrobenzene; and with cold aqueous potassium permanganate yielded valeric, butyric, propionic, and acetic acid; the non-volatile, acidic oxidation product, giving a positive Skraup colour reaction with aqueous ferrous sulphate and having ultraviolet absorption similar to those of simple alkylpyridinecarboxylic acids,[13] furnished, upon decarboxylation, a mixture of pyridine and its simple homologues. Like the lower homologue (III; R = Pr^n), the



$C_{15}H_{21}N$ base was extremely resistant to catalytic hydrogenation; however, reduction with sodium in boiling ethanol readily afforded a secondary base $C_{15}H_{27}N$ (VIII; R = H,

[11] Bowden, Braude, Jones, and Weedon, *J.*, 1946, 45.
[12] Swain, Eisner, Woodward, and Brice, *J. Amer. Chem. Soc.*, 1949, **71**, 1341.
[13] Plattner, Keller, and Boller, *Helv. Chim. Acta*, 1954, **37**, 1379.

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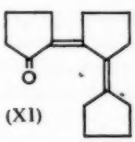
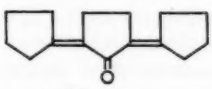
R′ = Bu^n) in which the original chromophore had been eliminated. This piperidine, which formed a chloroplatinate of indefinite composition, had an infrared spectrum very similar to that of *N*-*n*-butyl*cyclo*pentylamine (IX); in particular, a strong band at 1140 cm.$^{-1}$ appears to be characteristic of this class of compound. The *N*-methyl derivative (VIII; R = Me, R′ = Bu^n) prepared from the reduction product (VIII; R = H, R′ = Bu^n) by formaldehyde–formic acid was highly unstable, readily losing a basic gas (methylamine?) and leaving an intractable gum.

6-*n*-Butyl-2 : 3-4 : 5-di*cyclo*pentenopyridine was synthesised by the Tschitschibabin reaction [8] used by Goodman [2] for the preparation of the analogue (III; R = Pr^n). Our compound was produced in low yield from 2-*cyclo*pentylidene*cyclo*pentanone (I), valeraldehyde–ammonia, and ammonium acetate at 180°, together with (probably) 2-*n*-butyl-3 : 5-di-*n*-propylpyridine (X) arising by condensation of valeraldehyde and ammonia. Our compound (III; R = Bu^n) was also the principal basic product (12% yield) in a reaction at 250° between 2-(2′-*cyclo*pentylidene*cyclo*pentylidene)*cyclo*pentanone (XI) and ammonia in dioxan containing water (1 mol.) (in the absence of solvent and water, these reactants at 300° furnished little base).

The formation of the tricyclic product (III; R = Bu^n) from *cyclo*pentanone and ammonia entails condensation between three molecules of the ketone and one of ammonia, one of the C_5 rings opening; and in view of the rapidity with which *cyclo*pentanone self-condenses under base-catalysed conditions, formation of the ketone (XI) or its equivalent

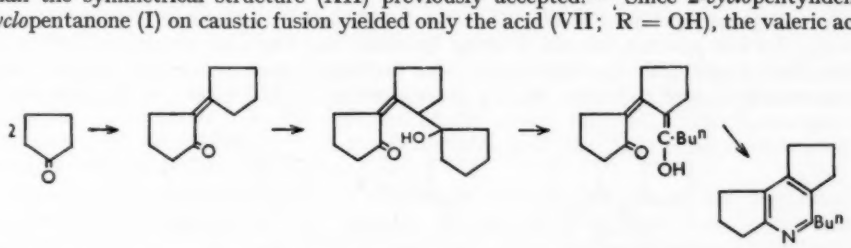


(XI)



(XII)

probably is an initial step. The fact that water appears to be essential in pyridine production from (XI) and ammonia suggests that a partial reversal of the aldol condensation is invoked at some stage—it is well established [14] that under conditions necessary for pyridine formation such reversals constitute one of the chief limitations of the Tschitschibabin pyridine synthesis and explain the formation of mixtures in many instances. Reversed aldol condensations seem to be involved in the production of valeric and δ-*cyclo*pent-1-enylvaleric (VII; R = OH) acid when the ketone (XI) is fused with potassium hydroxide at 260—280°, one of the reactions investigated by Mleziva [15] in proving structure (XI) for the tricyclic self-condensation product of *cyclo*pentanone, rather than the symmetrical structure (XII) previously accepted.[16] Since 2-*cyclo*pentylidene-*cyclo*pentanone (I) on caustic fusion yielded only the acid (VII; R = OH), the valeric acid



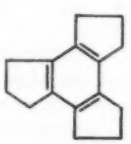
obtained from (XI) appears to originate from ring C, and, by analogy, the linear side-chain of the tricyclic base (III; R = Bu^n) originates from a similar source. The intramolecular

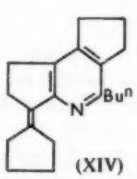
[14] Frank and Seven, *J. Amer. Chem. Soc.*, 1949, **71**, 2629.
[15] Mleziva, *Coll. Czech. Chem. Comm.*, 1954, **19**, 517.
[16] Wallach, *Ber.*, 1896, **29**, 2963; Goheen, *J. Amer. Chem. Soc.*, 1941, **63**, 744; Rosenfelder and Ginsburg, *J.*, 1954, 2957.

hydrogen-transfer required after the intermediate formation of (XI) or its partially-aldolised equivalent probably occurs under the stimulus of aromatisation, as annexed.

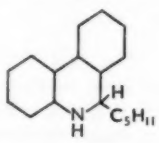
When *cyclo*pentanone (1·26 mol.) reacted with anhydrous ammonia (1 mol.) at 300°, the neutral products contained the ketones (I) and (XI), and tri*cyclo*pentenobenzene (XIII), all self-condensation products of *cyclo*pentanone. Whilst producing the base (III; R = Bu^n), this reaction also yielded a tertiary base $C_{20}H_{27}N$, which in addition to showing pyridine absorption maxima at 273 mμ (in MeOH) and at 284 mμ (in conc. HCl), had ultraviolet absorption at longer wavelengths [$\lambda_{inflex.}$ 310 mμ (in MeOH), $\lambda_{max.}$ 323—325 mμ (in conc. HCl)]. Catalytic hydrogenation completely removed this high wavelength absorption, whilst the principal pyridine absorption in the 275 mμ region was unaffected. Structures of type (XIV) in which a *cyclo*pentylidene system is conjugated with the pyridine nucleus seem likely.

Equimolecular quantities of *cyclo*hexanone and anhydrous ammonia under autogenous pressure at 300° furnished a moderate yield (33% of original weight of reactants) of a liquid tertiary base $C_{18}H_{27}N$ which formed a crystalline chloroplatinate, contained no active hydrogen, and resisted catalytic hydrogenation. Its infrared absorption spectrum had a strong band at 1570 $cm.^{-1}$ due to a heterocyclic nucleus, whilst the ultraviolet characteristics (Fig. 1) were those of compounds (III); hence by analogy with the base $C_{15}H_{21}N$, the structure (IV; R = n-C_5H_{11}) seemed probable. In support of this, permanganate oxidation yielded hexanoic, valeric, butyric, propionic, and acetic acid, whilst decarboxylation of the non-volatile acidic oxidation products gave a mixture of simple alkylbenzenes and pyridines. Sodium–ethanol reduction of the base $C_{18}H_{27}N$ furnished a secondary amine, presumably the perhydro-compound (XV). The formation of the base (IV; R = n-C_5H_{11}) from *cyclo*hexanone and ammonia is explicable, by analogy with the *cyclo*pentanone–ammonia condensation, on the basis of structure (XVI) established by

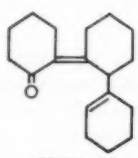

(XIII)



(XIV)



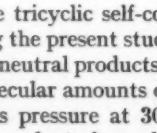
(XV)



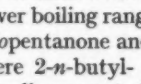
(XVI)

Mleziva [17] for the tricyclic self-condensation product of *cyclo*hexanone. No attempt has been made during the present studies to confirm structure (IV; R = n-C_5H_{11}) by synthesis.

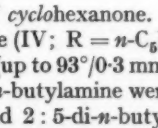
The principal neutral products of lower boiling range (up to 93°/0·3 mm.) from a reaction in which equimolecular amounts of *cyclo*pentanone and *n*-butylamine were heated together under autogenous pressure at 300° were 2-*n*-butyl- and 2 : 5-di-*n*-butyl-*cyclo*pentanone; another ketonic product, formed in small amount, had weak ultraviolet absorption at 220—230 mμ, probably associated with 2- or 3-alkyl*cyclo*pent-2-enones.[18] Infrared and ultraviolet spectra of the higher-boiling neutral products (93°/0·3 mm. to 180°/0·15 mm.)



(XVII)



(XVIII)



(XIX)

indicated the presence of both saturated and unsaturated *cyclo*pentanone derivatives, although no characteristic ketonic derivatives were isolated from these materials. The main constituent of the basic products from the *cyclo*pentanone–*n*-butylamine reaction

[17] Mleziva, *Coll. Czech. Chem. Comm.*, 1954, **19**, 505.
[18] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 72, 76; Gillam and West, *J.*, 1942, 486; Acheson and Robinson, *J.*, 1952, 1127.

XUM

(a small quantity of di-*n*-butylamine was detected) was a liquid tertiary base $C_{14}H_{19}N$ which formed a crystalline chloroplatinate. The ultraviolet spectrum of this base, which showed the pyridine-type bathochromic shift of maxima and minima on changing from neutral to acidic solvent,[12] was different from that of the base (III; R = Pr^n) (see Fig. 2). The infrared spectrum contained a principal band at 1592 cm.$^{-1}$ due to a heterocyclc nucleus, whilst –NH– and aromatic C–H stretching frequencies were absent; although a number of the infrared bands were found at similar wave-numbers to those in the spectrum of compound (III; R = Pr^n), there were some intensity differences. The mass spectrum was very similar to that given by the base (III; R = Pr^n). Thus this product probably has the isomeric structure (XVII). In chemical properties also this base closely resembled the analogue (III; R = Pr^n): oxidation afforded butyric, propionic, and acetic acid, whilst the non-volatile oxidation product had an ultraviolet spectrum similar to that of analogous material from the isomer (III; R = Pr^n). Sodium–ethanol reduction yielded the secondary perhydro-compound in which the original pyridine chromophore was destroyed: the infrared spectrum had a band in the 1140 cm.$^{-1}$ region characteristic of *N*-substituted *cyclo*pentylamines. It is of interest that a base of molecular weight 215 was detected in the mass spectrum of the *cyclo*pentanone–*n*-butylamine condensation base, although no material corresponding to molecular formula $C_{15}H_{21}N$ was isolable, probably because of the very small amount present. Such a compound could have been formed by interaction of *cyclo*pentanone with ammonia which was observed to be liberated during the reaction.

Compound (XVII) was synthesised in 11·5% yield from *cyclo*pentylamine and 3 mols. of 2-butylidene*cyclo*pentanone (XVIII) with a catalytic amount of ammonium acetate at 200°. Amongst the neutral products were 2-*n*-butyl*cyclo*pentanone (principal component) and 2-*cyclo*pentylidene*cyclo*pentanone (I), whilst there was mass-spectrometric evidence for 2 : 5-di-*n*-butyl*cyclo*pentanone and a butylidene- and a di-*n*-butyl-*cyclo*pentyl*cyclo*pentanone. In a second synthesis, *N*-(2-butylidene*cyclo*pentylidene)*cyclo*pentylamine (XIX) (1 mol.) [prepared by condensation of the ketone (XVIII) with *cyclo*pentylamine (cf. Norton *et al.*[19])] and 2-butylidene*cyclo*pentanone (2 mol.) were passed over activated alumina at 350°: the principal products were 2-*n*-butyl*cyclo*pentanone and the pyridine (XVII). The structure of the Schiff's base (XIX) was demonstrated by acid hydrolysis to the parent amine and ketone, and by hydrogenation to 2-*n*-butyldi*cyclo*pentylamine identical with the base obtained by reductive amination of 2-*n*-butyl*cyclo*pentanone with *cyclo*pentylamine.

In an attempt to investigate the materials responsible for the intense colour reaction with *p*-dimethylaminobenzaldehyde, the total neutral material from a reaction between *cyclo*pentanone and *n*-butylamine at 300° was hydrogenated over nickel at 200°/200 atm. The basic material (1·8% yield) isolated from the Ehrlich-negative product, which presumably contained reduction products of pyrrole-type substances, had ultraviolet absorption indicating a high proportion of the pyridine (XVII) which had been inadequately removed in the initial separation or, less probably, was produced by a molecular rearrangement in the presence of the nickel catalyst. Mass spectrometry indicated these reduced bases to be highly complex and since only small amounts were available this problem was not further studied.

After equimolecular amounts of *cyclo*pentanone and di-*n*-butylamine had been heated together under autogenous pressure at 300°, the neutral products of lower boiling-range (up to 88°/0·07 mm.), which had weak ultraviolet absorption in the 240 mμ region indicative of the presence of a 2 : 3-disubstituted *cyclo*pent-2-enone, were found to contain 2-*n*-butyl-*cyclo*pentanone and 2-*cyclo*pentyl*cyclo*pentanone (VI) as the main constituents. The higher-boiling neutral fractions (88°/0·1 mm. to 180°/0·4 mm.), from which no crystalline ketonic derivatives could be isolated, had infrared spectra indicating the presence of both saturated and unsaturated *cyclo*pentanone compounds, whilst their ultraviolet spectra

[19] Norton, Haury, Davis, Mitchell, and Ballard, *J. Org. Chem.*, 1954, **19**, 1054.

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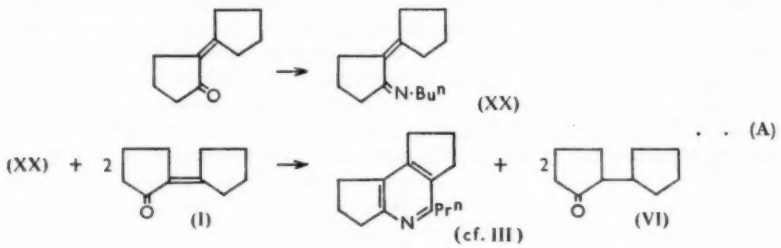
showed absorption at 228 and 257 mμ, suggesting 2- or 3-substituted *cyclo*pent-2-enones and compound (I). The basic reaction products contained much unchanged di-*n*-butylamine together with 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine (XVII). As for the *cyclo*pentanone–*n*-butylamine reaction, mass spectrometry provided some evidence for the presence of $C_{15}H_{21}N$ base derived from *cyclo*pentanone and ammonia, although again, no material of this composition could be isolated.

Reaction between equimolecular amounts of *cyclo*pentanone and tri-*n*-butylamine at 300° afforded much unchanged *cyclo*pentanone and its self-condensation products 2-*cyclo*pentylidene*cyclo*pentanone (I) and 2-(2′-*cyclo*pentylidene*cyclo*pentylidene)*cyclo*pentanone (XI). The basic material isolated was essentially unchanged tri-*n*-butylamine; however, a very small amount of material, b. p. 100—120°/0·4 mm., possessing spectra consistent with the presence of the base (XVII) was obtained.

Fission of a Bu^n–N link must have occurred during formation of the tricyclic base (XVII) from *cyclo*pentanone and *n*-butylamine or di-*n*-butylamine. The mechanism is obscure, but, in that connexion, two further reactions were investigated. *N-cyclo*Pentylidine-*n*-butylamine, the expected initial condensation product of *cyclo*pentanone and *n*-butylamine, was heated with 3 mol. of *cyclo*pentanone at 200° in the presence of ammonium acetate; the principal basic product was the pyridine (XVII), whilst the neutral components contained the *cyclo*pentanone derivatives (I), (VI), and (XI), together with *x*-*n*-butyl- and *x*-*cyclo*pentyl-2-*cyclo*pentylidene*cyclo*pentanone. The formation of the base (XVII) in this reaction may be consistent with intramolecular rearrangement of the Schiff's base before ring-closure to the heterocyclic system. The neutral products formed from 2-*cyclo*pentylidene*cyclo*pentanone (I) (2 mol.), *n*-butylamine (1 mol.), and a catalytic amount of ammonium acetate at 200° contained *cyclo*pentanone, 2-*cyclo*pentyl*cyclo*pentanone (VI), *x*-*n*-butyl-2-*cyclo*pentylidene*cyclo*pentanone, 2-(2′-*cyclo*pentylidene*cyclo*pentylidene)*cyclo*pentanone (XI), and *x*-*cyclo*pentyl-2-*cyclo*pentylidene*cyclo*pentanone. The presence of *cyclo*pentanone and the last two compounds indicates breakdown of 2-*cyclo*pentylidene*cyclo*pentanone (I) into cyclic C_5 units and it is from interaction of these smaller units with *n*-butylamine that the pyridine (XVII), which was produced unexpectedly in this condensation, must have been synthesised.

In connexion with the study of the thermal breakdown of *NN*′-di-*n*-butyladipamide,[1,2] we have investigated also a number of reactions, both catalysed and uncatalysed, between some *cyclo*pentanone compounds and *n*-butylamine in the vapour phase. As was first demonstrated by Dr. I. Goodman, lately of these laboratories, no production of carbon



dioxide, alkylated *cyclo*pentanones, pyrroles, or $C_{14}H_{19}N$ bases was observed when an equimolecular mixture of *cyclo*pentanone and *n*-butylamine was passed rapidly through a glass tube at 350°; however, *N-cyclo*pentylidene-*n*-butylamine was isolable in moderate yield. We found that an equimolecular mixture of 2-*cyclo*pentylidene*cyclo*pentanone (I) and *n*-butylamine under similar conditions gives a low yield of the resultant Schiff's base (XX) (its structure was proved by hydrolysis and hydrogenation). When, however, a similar reaction mixture was passed over activated alumina at 350°, the crude product, which gave a strong purple-red colour with *p*-dimethylaminobenzaldehyde reagent,

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contained some of the Schiff's base (XX), the pyridine (III; R = Pr^n), 2-*cyclo*pentyl*cyclo*pentanone (VI), and unchanged ketone (I). The formation of these products, and particularly (VI) and (III; R = Pr^n) in the approximate molecular ratio of 3·2 : 1, suggested that a base-catalysed hydrogen-transfer mechanism (cf. Weiss [20]) involving the Schiff's base and 2-*cyclo*pentylidene*cyclo*pentanone (I) may be operative (see annexed scheme). And when reaction (A) was investigated at 350° over activated alumina, the Ehrlich-positive product was shown to contain 2-*cyclo*pentyl*cyclo*pentanone (VI) and 6-*n*-propyl-2 : 3-4 : 5-di*cyclo*pentenopyridine (III; R = Pr^n) in the approximate molecular ratio of 2·5 : 1, which is in good agreement with the 2 : 1 stoicheiometry considering the difficulty in assessing the true yields.

The vapour-phase reaction between *cyclo*pentanone and *n*-butylamine in the presence of activated alumina at 350° yielded an Ehrlich-positive product containing *N-cyclo*pentylidene-*n*-butylamine and the previous products (XX) and (XVII); infrared examination showed the neutral components to be complex but to contain the ketones (I) and (VI) as principal products. In contrast to the uncatalysed vapour-phase reaction, only a trace of unchanged *cyclo*pentanone was recovered.

An abstract of a memoir by Zelinski and Shuikin [21] indicates that *cyclo*pentanone, when passed in the vapour phase over activated alumina at 200°, gives 2-*cyclo*pentylidene*cyclo*pentanone (I) in 41% yield unaccompanied by higher self-condensation products: in our experience 2-*cyclo*pentylidene*cyclo*pentanone prepared by this procedure always contains the tricyclic self-condensation product (XI) of *cyclo*pentanone, even from reaction at temperatures as low as 130° (the b. p. of *cyclo*pentanone). For the preparation of the relatively large quantities of the bicyclic ketone (I) required in this investigation Mleziva's preparation [15] of the tricyclic ketone (XI) from *cyclo*pentanone by the action of potassium hydroxide was suitably modified.

Experimental

Ultraviolet absorption spectra were measured on a Cary self-recording spectrophotometer. Infrared spectra were recorded on a Grubb-Parsons double-beam spectrometer (Model S4) with rock-salt optics. Autoclave experiments were conducted in a stainless-steel (18 : 8 : 1 : 1) vessel, of 750 ml. capacity, heated in a metal-bath. Paper chromatograms (Whatman No. 1 paper) of aliphatic acids were run, by the ascending technique, in butan-1-ol saturated with 1·5N-aqueous ammonia; spots were located by the conventional ethanolic Bromocresol Green indicator.

cyclo*Pentanone*.—Thorpe and Kon's procedure [22] was used for the preparation of large quantities of this ketone, which had b. p. 130—131°, n_D^{20} 1·4365 (Goheen [16] gives b. p. 130·7—130·8°/765 mm., n_D^{20} 1·43704).

Self-condensation of cyclo*Pentanone*.—(a) *In the vapour phase over activated alumina. cyclo*Pentanone (1574 g.) was allowed to drip during 30 hr. down a vertical column (32 cm. × 2 cm. diam.) of granular activated alumina (4—8 mesh) at 150° ± 10°. Distillation of the dried (Na_2SO_4) condensate gave fractions (1) (550 g.) b. p. 128—136°/760 mm., (2) (168 g.) b. p. 36°/22 mm., (3) (441 g.) b. p. 126°/16 mm., (4) (11 g.) b. p. 72—120°/0·14 mm., and (5) (91 g.) b. p. 140—141°/0·14 mm. Fractions (1) and (2) were unchanged *cyclo*pentanone. Fraction (3) was 2-*cyclo*pentylidene*cyclo*pentanone (I), a pale yellow oil, n_D^{20} 1·5218, $\lambda_{max.}$ 257 mμ (log ε 4·10 in MeOH) [Wallach [16] gives b. p. 117—119°/12 mm., n_D^{20} 1·52095; French and Wiley [23] report $\lambda_{max.}$ 259 mμ (log ε 4·03 in EtOH)]. The 2 : 4-dinitrophenylhydrazone of 2-*cyclo*pentylidene-*cyclo*pentanone separated from much methanol or ethyl acetate in maroon needles, m. p. 229—230° (decomp.) (lit.,[24] m. p. 228—229°). The semicarbazone of ketone (I) formed needles, m. p. 205°, from methanol (Wallach [16] records m. p. 200—205°; Kon and Nutland [25] gives m. p.s

[20] Weiss, *J. Amer. Chem. Soc.*, 1952, **74**, 200.
[21] Zelinski and Shuikin, *J. Russ. Phys. Chem. Soc.*, 1930, **62**, 1343; *Chem. Abs.*, 1931, **25**, 2420.
[22] Thorpe and Kon, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 192.
[23] French and Wiley, *J. Amer. Chem. Soc.*, 1949, **71**, 3702.
[24] Marvel and Brookes, *ibid.*, 1941, **63**, 2853.
[25] Kon and Nutland, *J.*, 1926, 3106.

223° and 207° respectively for the two forms of this derivative). Fraction (5) was 2-(2′-*cyclo*pentylidene*cyclo*pentylidene)*cyclo*pentanone (XI), which separated from aqueous methanol in massive yellow rhombic plates and from light petroleum (b. p. 60—80°) in long yellow needles, m. p. 80°, $\lambda_{max.}$ 301 mμ (log ε 4·46 in MeOH) [Mleziva [15] gives b. p. 165—183°/5 mm., m. p. 79°, $\lambda_{max.}$ 300, 366 mμ (log ε 4·44, 2·45)]. The C=O absorption was at 1692 cm.$^{-1}$ (Nujol mull).

(b) *In the presence of powdered potassium hydroxide.* *cyclo*Pentanone (500 g.) was boiled under reflux in the presence of powdered potassium hydroxide (2·5 g.), and liberated water (55 ml.) was removed (Dean–Stark). The cooled mixture was treated with saturated aqueous sodium chloride (500 ml.), then extracted with ether (8 × 50 ml.). Distillation of the product gave fractions (1) (60 g.) b. p. 40—110°/20 mm. and (2) (213 g.) b. p. 110—136°/20 mm., and a high-boiling residue (119 g.). Fractions (1) and (2) were essentially *cyclo*pentanone and 2-*cyclo*pentylidene*cyclo*pentanone respectively. The crystalline residue had b. p. 141—150°/0·12 mm., and, when recrystallised from aqueous methanol, furnished the ketone (XI) as massive yellow rhombs (103 g.), m. p. 80°.

2-cyclo*Pentyl*cyclo*pentanone* (VI).—Hydrogen (0·94 mol.) was absorbed when 2-*cyclo*pentylidene*cyclo*pentanone (150 g.) in dioxan (200 ml.) was hydrogenated at 100°/100 atm. over nickel–kieselguhr (15 g.). Distillation of the residue remaining after removal of the catalyst and solvent afforded 2-*cyclo*pentyl*cyclo*pentanone (VI) (125 g.), b. p. 120—121°/25·5 mm., n_D^{23} 1·4768 (Found: C, 78·7; H, 10·6. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·6%) (lit.: b. p. 117—120°/16 mm., n 1·4763; [26] b. p. 107—109°/13 mm., n_D^{20} 1·4772 [27]). The C=O absorption band was at 1730 cm.$^{-1}$ (Cherrier [28] gives 1718 cm.$^{-1}$). The semicarbazone formed needles, m. p. 208—209°, from methanol (Found: C, 63·7; H, 9·4; N, 19·7. Calc. for $C_{11}H_{19}ON_3$: C, 63·1; H, 9·2; N, 20·1%) (lit., m. p. 210°,[21, 26] 209° [27]). The 2 : 4-dinitrophenylhydrazone separated from methanol in orange needles, m. p. 158° (Found: C, 58·2; H, 5·8; N, 16·9. Calc. for $C_{16}H_{20}O_4N_4$: C, 57·8; H, 6·1; N, 16·9%) (lit.,[29] m. p. 158—159°).

6-n-*Butyl*-2 : 3-4 : 5-*di*cyclo*pentenopyridine* (III; R = Bu^n).—(a) *Synthesis from* 2-cyclo*pentylidene*cyclo*pentanone and valeraldehyde–ammonia.* 2-*cyclo*Pentylidene*cyclo*pentanone (150 g.), valeraldehyde–ammonia [obtained by passing anhydrous ammonia (19·5 g.) into valeraldehyde (172 g.) at −5° to −10°], and ammonium acetate crystals (10 g.) were heated together under autogenous pressure (max. was 270 lb./sq. in.) at 180° ± 2° with continuous stirring during 10 hr. The cold product was isolated from the bomb with methanol (100 ml.), ether (500 ml.) was added, and the resulting solution then washed with 2N-sulphuric acid (12 × 100 ml.). After liberation with 40% aqueous sodium hydroxide, the basic product was isolated from this aqueous extract with ether (6 × 100 ml.), and, after solvent had been removed, was treated for 1 hr. with acetic anhydride (105 ml.) containing concentrated sulphuric acid (1 ml.). The cooled mixture was added to water (1000 ml.) and, 2 hr. later, was basified by the careful addition of soda ash and extracted with ether (6 × 100 ml.). After isolation from the ethereal solution with 2N-sulphuric acid, the non-acetylated basic product was distilled and yielded: fractions (1) (19·69 g.) b. p. 92—133°/2·3 mm.; (2) (10·77 g.) b. p. 142—143°/2·3 mm., and (3) (12·55 g.) b. p. 148—150°/2·3 mm.

Fraction (1) was mainly 2-n-*butyl*-3 : 5-*di*-n-*propylpyridine* (X) (13·02 g.), b. p. 79°/0·07 mm., n_D^{22} 1·5009 (Found: C, 82·7; H, 11·2; N, 7·0. $C_{15}H_{25}N$ requires C, 82·1; H, 11·5; N, 6·4%); $\lambda_{max.}$ 271 mμ (log ε 3·72), $\lambda_{infl.}$ 279 mμ (log ε 3·65), and $\lambda_{min.}$ 237 mμ (log ε 2·84 in MeOH); $\lambda_{max.}$ 277 mμ (log ε 3·96), $\lambda_{infl.}$ 240 mμ (log ε 2·93), and $\lambda_{min.}$ 246 mμ (log ε 2·86) in conc. HCl; $\nu_{max.}$ 1605m, 1580m, and 1565m (pyridine ring), and at 2933—2865s, 1464—1453s, and 1381 cm.$^{-1}$ (CH_2 and Me).

Fraction (2) was redistilled; material of b. p. <91°/0·06 mm. was rejected whilst the component (3·27 g.), b. p. 91—96°/0·06 mm., n_D^{22} 1·5340, was combined with (3). Fractionation of this combined product then gave: (4) (1·28 g.) b. p. 92—94°/0·06 mm., n_D^{22} 1·5346; (5) (3·29 g.) b. p. 94°/0·06 mm., n_D^{22} 1·5350; and (6) (9·43 g.) b. p. 94°/0·06 mm., n_D^{22} 1·5360. Repeated redistillation of fraction (6) afforded 6-n-*butyl*-2 : 3-4 : 5-*di*cyclo*pentenopyridine* (III; R = Bu^n), a pale yellow oil (Found: C, 84·0, 83·8; H, 10·1, 10·0; N, 6·5, 7·1. $C_{15}H_{21}N$ requires C, 83·7; H, 9·8; N, 6·5%); $\lambda_{max.}$ 275 mμ (log ε 3·81), $\lambda_{min.}$ 239—240 mμ (log ε 2·86) in MeOH; $\lambda_{max.}$ 227,

[26] Wallach, *Annalen*, 1912, **389**, 179.
[27] Turova-Pollak, Sosnina, and Treshchova, *Zhur. obshchei Khim.*, 1953, **23**, 1111; *Chem. Abs.*, 1953, **47**, 12207.
[28] Cherrier, *Compt. rend.*, 1947, **225**, 997.
[29] Cordon, Knight, and Cram, *J. Amer. Chem. Soc.*, 1954, **76**, 1646.

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284 mμ (log ε 3·57, 4·03), $\lambda_{infl.}$ 237 mμ (log ε 3·45), and $\lambda_{min.}$ 250 mμ (log ε 2·78) in conc. HCl; $\nu_{max.}$ 1605s and 1585s (pyridine ring), and 2959—2841s, 1460s, and 1379ms cm.$^{-1}$ (CH_2 and Me). The mass spectrum was characterised by peaks at mass : charge ratios 215 and 173. The *chloroplatinate*, orange needles from chloroform–light petroleum (b. p. 60—80°), had m. p. 184° (decomp.) after desolvation at 100° for 18 hr. [Found: C, 42·4; H, 5·3; N, 3·2; Cl, 26·1; Pt (ash), 24·0. $C_{30}H_{44}N_2Cl_6Pt$ requires C, 42·9; H, 5·3; N, 3·3; Cl, 25·3; Pt, 23·2%].

(b) *Synthesis from* 2-(2′-cyclo*pentylidene*cyclo*pentylidene*)cyclo*pentanone and ammonia.* The ketone (XI) (108 g.) in purified dioxan (120 ml.) containing water (9·0 g.) was heated with anhydrous ammonia (8·5 g.) in an autoclave kept at 248° ± 2° during 6 hr. (max. pressure was 800 lb./sq. in.); agitation was continuous throughout. Solvent was removed by distillation, and the viscous black residue was dissolved in chloroform (500 ml.), washed with 2N-sulphuric acid (6 × 100 ml.), and set aside over Na_2SO_4. After being washed with chloroform (4 × 100 ml.) (these washings were combined with the chloroform solution of neutral reaction products), the acidic extracts were basified and the liberated bases, isolated with ether (8 × 75 ml.), were distilled and furnished 6-*n*-butyl-2 : 3-4 : 5-di*cyclo*pentenopyridine (13·4 g.), b. p. 112—114°/0·14 mm., n_D^{22} 1·5366 (Found: C, 83·2, 83·2; H, 9·1, 9·5; N, 6·1, 6·5%). This material had a mass spectrum and ultraviolet and infrared absorption identical with those of the base (III; R = Bu^n) synthesised by route (a). The chloroplatinate had m. p. and mixed m. p. 182—183° (decomp.) [Found: C, 42·7; H, 5·3; N, 3·4; Cl, 25·7; Pt (ash), 23·0%]. The *X*-ray powder photographs of the chloroplatinates were identical.

When distilled, the viscous black residue (84·0 g.) which remained after evaporation of the dried chloroform solution of neutral material yielded an oil (0·4 g.), b. p. 100—125°/25 mm., essentially 2-*cyclo*pentyl*cyclo*pentanone (semicarbazone, m. p. and mixed m. p. 207°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 156°).

6-n-*Butyl*-2 : 3-4 : 5-*di*cyclo*pentanopiperidine* (VIII; R = H, R′ = Bu^n).—Sodium (6·5 g.) was added in pieces during 2—3 hr. to a solution of the pyridine derivative (III; R = Bu^n) (3·04 g.) in boiling ethanol (30 ml.). After 18 hours' heating, unchanged sodium was destroyed by ethanol (30 ml.), some of the solvent was distilled off, the residue was poured into water (300 ml.), and the resulting deep-yellow solution was extracted with ether (6 × 50 ml.). The ethereal extracts were washed with 2N-hydrochloric acid (4 × 50 ml.), the washings basified with 20% aqueous sodium hydroxide, and the liberated base, isolated with ether, was distilled and yielded 6-n-*butyl*-2 : 3-4 : 5-*di*cyclo*pentanopiperidine* as a colourless oil (2·58 g.), b. p. 101—102°/0·35 mm., n_D^{23} 1·4996, which gave a blue colour with sodium nitroprusside–acetaldehyde [30] (Found: C, 81·1; H, 12·1; N, 6·9. $C_{15}H_{27}N$ requires C, 81·4; H, 12·3; N, 6·3%). Light absorption was not significant at wavelengths greater than 230 mμ. The infrared spectrum had bands at 3425m and 1149ms (ring –NH–), and at 2985—2195s, 1460s, and 1379ms cm.$^{-1}$ (CH_2 and Me). The mass spectrum contained a series of peaks at mass : charge ratios 221, 206, 192, 178, 164, 150, and 138.

The chloroplatinate of (VIII; R = H, R′ = Bu^n) separated from chloroform–light petroleum (b. p. 60—80°) in orange needles, which, after desolvation at 100°/0·2 mm. during 4 hr., had m. p. 200—201° (decomp. at 203°). This material gave unsatisfactory analyses.

6-*n*-Butyl-2 : 3-4 : 5-di*cyclo*pentanopiperidine (1·0 g.) was heated at 100° during 24 hr. with 40% aqueous formaldehyde (5·0 ml.) and formic acid (12·0 ml.), and the mixture then cooled, poured into water (150 ml.), and basified with 2N-sodium hydroxide. Isolated with ether (6 × 50 ml.), the 1-*methyl derivative* (VIII; R = Me, R′ = Bu^n) was obtained as a colourless oil (0·77 g.), b. p. 120°/0·5 mm., n_D^{23} 1·5000, which gave no colour with nitroprusside–acetaldehyde reagent (Found: N, 6·1; *N*-Me, 12·6. $C_{16}H_{29}N$ requires N, 5·95; 1*N*-Me, 12·3%). Satisfactory carbon and hydrogen analyses were not obtained on this material, which rapidly decomposed with the evolution of methylamine (?) and the formation of a tar.

Oxidation of 6-n-*Butyl*-2 : 3-4 : 5-*di*cyclo*pentenopyridine.*—Finely powdered potassium permanganate (26 g.) was added portionwise during 4 hr. to a stirred suspension of the base (III; R = Bu^n) (4·0 g.) in water (600 ml.) at 20°; stirring was then continued for a further 48 hr. The precipitated manganese dioxide was collected and washed with water, and the combined filtrate and washings were clarified with sulphur dioxide. The yellow solution was continuously extracted with ether during 16 hr., and the viscous residue (3·75 g.), isolated from the dried ethereal extract, was evaporated at 0·05 mm. from a water-bath (temp. from 20° to

[30] (*a*) Feigl and Anger, *Mikrochim. Acta*, 1937, **1**, 138; (*b*) Feigl, "Spot Tests," Vol. II. Organic Applications," Elsevier, Amsterdam, 1954, p. 189.

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100°). The volatile products (0·49 g.), collected in a trap at −80°, were shown by paper chromatography to be a mixture of valeric, butyric, propionic, and acetic acid, whilst the non-volatile oxidation products (3·16 g.) gave an orange-yellow colour with aqueous ferrous sulphate and had a light absorption max. (in MeOH) at 280 and a min. at 260 mμ.

A solution of the non-volatile oxidation product in water (30 ml.) was made alkaline (Brilliant Yellow) by saturated aqueous barium hydroxide and evaporated. The finely powdered barium salts were mixed with soda-lime (40 g.) and copper bronze (3 g.), and pyrolysed at red-heat. The products of decarboxylation, which steam-distilled from the retort with the water liberated in the reaction, were isolated from the distillate by continuous ether-extraction during 24 hr., and when fractionated gave fractions: (1) (0·65 g.) b. p. 68—100°/36 mm., $\lambda_{max.}$ 261, 267 mμ ($E^{1\%}_{1\,cm.}$ 200·5, 173), $\lambda_{infl.}$ 256 mμ ($E^{1\%}_{1\,cm.}$ 177), $\lambda_{min.}$ 266 mμ ($E^{1\%}_{1\,cm.}$ 171) (in MeOH); (2) (0·17 g.) b. p. 70—100°/0·08 mm., $\lambda_{max.}$ 260, 267 mμ ($E^{1\%}_{1\,cm.}$ 247, 243) (in MeOH). Fraction (1) was a mixture of substituted pyridines and benzenes with the former predominant (mass and infrared spectra).

High-temperature Reactions of cyclo*Pentanone and Related Compounds with Aliphatic Bases under Autogenous Pressure: General Procedure.*—The appropriate ketones and bases were heated (see below) under the conditions summarised in Table 1. After cooling, the product which generally was a dark viscous gum giving an intense purple colour with Ehrlich's *p*-dimethylaminobenzaldehyde reagent, was removed from the autoclave with ether (500 ml.). Two hours later, any aqueous phase was separated and the ethereal solution was extracted with N-sulphuric acid (8 × 100 ml.) and set aside over Na_2SO_4. The combined acidic extracts were washed with ether (6 × 50 ml.) (these washings were added to the ethereal solution of non-basic products), basified to Brilliant Yellow with 20% aqueous sodium hydroxide, and extracted with ether for 24 hr. The dried extracts of basic and non-basic materials were then evaporated, and each was examined in detail by the methods described below. In Expt. 2, the crude product was fractionally distilled before chemical separation was effected.

Reaction of cyclo*Pentanone with Anhydrous Ammonia at* 300° (Table 1; Expt. 1).—(a) *Non-basic products.* Distillation of the crude material gave: (1) (1·46 g.) b. p. 62—70°/0·3 mm., n_D^{22} 1·4870; (2) (2·84 g.) b. p. 70—102°/0·2 mm., n_D^{22} 1·5079; (3) (4·00 g.) b. p. 102—140°/0·2 mm., a partly crystalline, pale yellow oil; and a black pitch (12·83 g.). Fractions (1) and (2) were mixtures of 2-*cyclo*pentyl*cyclo*pentanone (semicarbazone, m. p. and mixed m. p. 207°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 154°) and 2-*cyclo*pentylidene*cyclo*pentanone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229° (decomp.)]; traces of nitrile were also present (infrared spectrum).

Ether (5 ml.) was added to fraction (3) and the crystalline product was filtered off. Recrystallised from much ether, this *substance* separated in colourless plates (75 mg.), m. p. 114—115° (Found: C, 67·7; H, 9·7; N, 8·0. $C_{16}H_{17}ON,\frac{1}{2}H_2O$ requires C, 68·1; H, 10·3; N, 7·95%. $C_{16}H_{17}ON$ requires C, 71·8; H, 10·25; N, 8·4%), having infrared absorption bands at

TABLE 1. *Condensation of* cyclo*pentanone and related compounds with aliphatic bases under autogenous pressure.*

Expt.	Reactants: Ketone, g. (mole)	Base, g. (mole)	Max. temp.	Time at max. temp. (hr.)	Max. pressure (lb./sq. in.)	H_2O layer removed (g.)
1	*cyclo*Pentanone 125 (1·49)	NH_3 25 (1·78)	300° ± 5°	6	1250	24·8
2	*cyclo*Pentanone 125 (1·49)	NH_3 20 (1·18)	300 ± 5	6	—	—
3	*cyclo*Hexanone 130 (1·325)	NH_3 22·5 (1·325)	300 ± 5	6	820	22·8
4	*cyclo*Pentanone 84 (1·0)	NH_2Bu 73 (1·0)	300 ± 5	6	850	15·0
5	*cyclo*Pentanone 84 (1·0)	$NHBu_2$ 129 (1·0)	300 ± 5	6	450	4·8
6	*cyclo*Pentanone 84 (1·0)	NBu_3 185 (1·0)	300 ± 5	6	275	3·2
7	*cyclo*Pentanone 91·5 (1·09)	*N-cyclo*Pentylidene-*n*-butylamine 49 (0·352)	206 ± 8	10	NH_4OAc cryst. (6·8 g.) added	
8	2-*cyclo*Pentylidene*cyclo*pentanone 185 (1·235)	NH_2Bu 30 (0·411)	200 ± 5	10	240	NH_4OAc cryst. (10 g.) added

3360, 3180, and 1650 cm.$^{-1}$ (—CO·NH_2). Fraction (3) (7·3 g. from 2 expts.) in methanol (10 ml.) was hydrolysed during 20 hr. with boiling 40% aqueous potassium hydroxide (10 ml.). Ammonia was evolved, and from the acidified hydrolysate there was isolated an acid, a pale yellow oil (0·41 g.), b. p. 121°/0·1 mm., n_D^{22} 1·4787 (Found: C, 70·9; H, 10·0. Calc. for $C_{10}H_{16}O_2$:

C, 71·4; H, 9·6%) (Mleziva [15] reports b. p. 131—133°/3 mm., n_D^{20} 1·4662, for δ-*cyclo*pent-1 enylvaleric acid).

(b) *Basic products.* When fractionated, the crude material yielded: (4) (25·89 g.) b. p. 121—122°/0·7 mm., n_D^{22} 1·5368; (5) (3·80 g.) b. p. 125—142°/0·5 mm., n_D^{22} 1·5385; (6) (4·04 g.) b. p. 162—168°/0·5 mm., n_D^{22} 1·5442; an involatile pitch (37·0 g.) remained. Fraction (4) was mainly 6-*n*-butyl-2 : 3-4 : 5-di*cyclo*pentenopyridine, b. p. 108—110°/0·1 mm., 120°/0·5 mm., n_D^{22} 1·5366 [Found: C, 83·5, 83·6, 83·8, 84·2; H, 9·8, 9·1, 9·6, 9·6; N, 6·5, 6·5, 6·9, 7·0; active H, 0·03%; equiv. (potentiometrically), 216·3, 216·4. Calc. for $C_{15}H_{21}N$: 1 active H, 0·47%; equiv., 215·3], which gave a chloroplatinate, m. p. and mixed m. p. 182—183° (decomp.) [Found, in sample dried at 100°/0·2 mm.: C, 43·0, 42·9; H, 5·3, 5·0; N, 3·1, 3·4; Cl, 25·5, 26·1; Pt(ash), 23·4%]. The identity of the base was confirmed further by spectra (light, infrared, and mass), by sodium–ethanol reduction to the piperidine (VIII; R = H, R′ = Bu^n), b. p. 92—94°/0·2 mm., n_D^{22} 1·4999 [Found: C, 81·8; H, 12·1; N, 6·2; active H, 0·43%; equiv. (potentiometrically), 220·3. Calc. for $C_{15}H_{27}N$: H, 0·42%; equiv., 221·4] (mass and infrared spectra), and by oxidation with aqueous potassium permanganate.

Reaction of cyclo*Pentanone* (*Excess*) *with Anhydrous Ammonia at* 300°. (Table 1; Expt. 2).—The total product was distilled and yielded: (1) (15·84 g.) b. p. 42°/64 mm.; (2) (10·41 g.) b. p. 123—130°/16 mm.; (3) (24·19 g.) b. p. 126°/0·15 mm. to 131°/0·28 mm.; (4) (4·07 g.) b. p. 148—156°/0·28 mm.; (5) (25·86 g.) b. p. 172—186°/0·35 mm.; an involatile residue (26·01 g.) was left. Fraction (1) was water. Fraction (2) was mainly 2-*cyclo*pentylidene*cyclo*pentanone [semicarbazone, m. p. and mixed m. p. 204—205°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229—230° (decomp.)]. Fraction (3) was separated into basic and non-basic constituents with ether and N-sulphuric acid in the usual way. The basic component yielded 6-*n*-butyl-2 : 3-4 : 5-di*cyclo*pentopyridine (19·96 g.) [Found: C, 84·2; H, 9·8; N, 7·0%; equiv. (B.D.H. " 4·5 " indicator), 219·1] (light and infrared spectra); the chloroplatinate, after desolvation at 100°/0·2 mm. for 6 hr., had m. p. and mixed m. p. 182—183° (decomp.). Fractionation of the non-basic component (3·42 g.) of fraction (3) yielded five arbitrary, Ehrlich-positive sub-fractions: (*a*) (0·50 g.) b. p. 69—79°/0·45 mm., n_D^{22} 1·5208; (*b*) (0·62 g.) b. p. 84—86°/0·45 mm., n_D^{22} 1·5225; (*c*) (0·23 g.) b. p. 90—104°/0·3 mm., n_D^{22} 1·5322; (*d*) (1·15 g.) b. p. 108—120°/0·4 mm., n_D^{22} 1·5430; (*e*) (0·68 g.) b. p. 120—130°/0·4 mm., n_D^{22} 1·5527. (*a*), (*b*), and (*c*) were recombined and gave 2-*cyclo*pentylidene*cyclo*pentanone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229° (decomp.)]. Sub-fractions (*d*) and (*e*) were mixtures containing 2-*cyclo*pentylidene-*cyclo*pentanone, the ketone (XI), and tri*cyclo*pentenobenzene (light, infrared, and mass spectra); traces of nitrogenous products were also present.

After recombination, fractions (4) and (5) were separated by the usual procedure into basic and non-basic components. Distillation of the non-basic constituents (5·0 g.) yielded three Ehrlich-positive sub-fractions: (*f*) (0·42 g.) b. p. 40—136°/0·2 mm., n_D^{22} 1·5237; (*g*) (1·68 g.) b. p. 138—150°/0·2 mm., n_D^{22} 1·5557; (*h*) (2·26 g.) b. p. 150—164°/0·2 mm., n_D^{22} 1·5641. Sub-fraction (*f*) was essentially 2-*cyclo*pentylidene*cyclo*pentanone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229—230° (decomp.)]. Both sub-fractions (*g*) and (*h*) contained, *inter alia*, 2-*cyclo*-pentylidene*cyclo*pentanone, the ketone (XI), and tri*cyclo*pentenobenzene; traces of nitrogenous compounds were present also.

The basic components (23·3 g.) of fractions (4) and (5) were distilled and gave two sub-fractions (green-yellow oils): (*m*) (8·72 g.) b. p. 152°/0·1 mm. to 172°/0·2 mm., n_D^{22} 1·5482; (*n*) (5·46 g.) b. p. 172—186°/0·2 mm., n_D^{22} 1·5779. Sub-fraction (*m*) (Found: C, 85·2; H, 9·4; N, 5·6. Calc. for $C_{20}H_{27}N$: C, 85·35; H, 9·7; N, 5·0%) had $\lambda_{max.}$ 273 mμ ($E^{1\%}_{1\,cm.}$ 246), $\lambda_{infl.}$ 310 mμ ($E^{1\%}_{1\,cm.}$ 47·4), $\lambda_{min.}$ 235—237 mμ ($E^{1\%}_{1\,cm.}$ 83) in MeOH; $\lambda_{max.}$ 224—229, 284, and 341—344 mμ ($E^{1\%}_{1\,cm.}$ 208, 361, and 89); $\lambda_{infl.}$ 237 mμ ($E^{1\%}_{1\,cm.}$ 186), and $\lambda_{min.}$ 253—255, 323—325 mμ ($E^{1\%}_{1\,cm.}$ 93, 71) in conc. HCl. When hydrogenated in the presence of platinum oxide (50 mg.), sub-fraction (*m*) (534 mg.) absorbed hydrogen (0·75 mol.) and the resulting base (in MeOH) had $\lambda_{max.}$ 275 mμ ($E^{1\%}_{1\,cm.}$ 225) and $\lambda_{min.}$ 239—244 mμ ($E^{1\%}_{1\,cm.}$ 40) with absorption in the region above 300 mμ completely eliminated.

Reaction of cyclo*Hexanone with Anhydrous Ammonia at* 300° (Table 1; Expt. 3).—(a) *Basic products.* When distilled, the total crude basic material (110·5 g.) afforded three fractions, all pale yellow oils; (1) (2·13 g.) b. p. 40—138°/0·10 mm., n_D^{23} 1·5320; (2) (50·90 g.) b. p. 138—146°/0·10 mm., n_D^{23} 1·5400; (3) (13·17 g.) b. p. 146—170°/0·10 mm., n_D^{23} 1·5412; an involatile pitch (42·30 g.) remained.

Fraction (2) was mainly 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*octahydro*-9-n-*pentylphenanthridine* (IV;

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R = *n*-C_5H_{11}), a viscous green-yellow, slightly fluorescent oil, b. p. 142°/0·10 mm., n_D^{23} 1·5411 [Found: C, 83·9; H, 10·7; N, 5·7; active H, 0·036%; equiv. (potentiometrically), 253·6. $C_{18}H_{27}N$ requires C, 84·0; H, 10·6; N, 5·4; 1 H, 0·39%; equiv., 257·4]; $\lambda_{max.}$ 273 mμ (log ε 3·69), $\lambda_{min.}$ 242 mμ (log ε 2·91) in MeOH; $\lambda_{max.}$ 225—227, 281 mμ (log ε 3·56, 3·97), $\lambda_{min.}$ 249 mμ (log ε 2·52) in conc. HCl. The infrared spectrum showed bands at 1570s (pyridine ring), and at 2950—2850s, 1462s, 1442s, and 1380 cm.$^{-1}$ (CH_2 and Me). The *chloroplatinate* of this base separated from chloroform–light petroleum (b. p. 60—80°) in orange needles, which after desolvation at 100°/0·2 mm. during 16 hr., had m. p. 189—190° (decomp.) [Found: C, 46·6; H, 5·9; N, 2·7; Cl, 22·7; Pt(ash), 21·0. $C_{36}H_{56}N_2Cl_6Pt$ requires C, 46·75; H, 6·1; N, 3·0; Cl, 23·0; Pt, 21·1%]. Reduction of the base (IV; R = *n*-C_5H_{11}) (7·5 g.) with sodium (15·0 g.) and ethanol (75 ml.) by the usual procedure furnished *perhydro*-9-n-*pentylphenanthridine* (XV) (5·72 g.), b. p. 136—138°/0·1 mm., n_D^{23} 1·5084 (Found: C, 82·2; H, 12·1; N, 5·9. $C_{18}H_{33}N$ requires C, 82·1; H, 12·6; N, 5·3%), which gave a blue colour with nitroprusside–acetaldehyde reagent.

The base (IV; R = *n*-C_5H_{11}) (8·0 g.) in aqueous suspension (700 ml.) with potassium permanganate (55 g.) at room temperature during 6 days gave volatile acids (1·05 g.) shown by paper chromatography to include hexanoic, valeric, butyric, propionic, and acetic acid. The non-volatile oxidation products (6·21 g.), which gave an orange colour with aqueous ferrous sulphate and had $\lambda_{max.}$ 284 mμ, $\lambda_{min.}$ 260 mμ (in MeOH), were converted into the mixed barium salts (9·65 g.) and then pyrolysed at red heat with soda-lime (40 g.) and copper bronze (3 g.). Distillation of the decarboxylated material gave: (i) (0·20 g.) b. p. 70—90°/32 mm., $\lambda_{max.}$ 261, 268 mμ ($E_{1\,cm.}^{1\%}$ 176·5, 149), $\lambda_{infl.}$ 256, 266 mμ ($E_{1\,cm.}^{1\%}$ 160, 146) in MeOH; (ii) (0·10 g.) b. p. 80—90°/0·1 mm. Fraction (i) had a mass spectrum which indicated the presence of the following benzenes and pyridines: C_6H_6, C_7H_8, C_8H_{10}, C_5H_5N, and C_6H_7N; the peaks due to benzene and its homologues were considerably larger than those due to the accompanying pyridines. The infrared spectrum was similar to that given by analogous mixed bases derived from 6-*n*-butyl-2 : 3-4 : 5-di*cyclo*pentenopyridine.

Fraction (3) had light absorption characteristics very similar to those of the pure base (IV; R = *n*-C_5H_{11}) but showed additional weak absorption in the region 300—340 mμ.

(b) *Non-basic products.* Distillation of this material (17·30 g.) afforded: (4) (2·61 g.) b. p. 67°/20 mm., n_D^{23} 1·4539; (5) (3·24 g.) b. p. 80—120°/0·10 mm., n_D^{23} 1·4822; both these fractions showed weak light absorption in the range 220—260 mμ but were not studied further.

N-n-*Butyl*cyclo*pentylamine* (IX) (with I. Goodman).—Hydrogen (0·97 mol.) was absorbed when *cyclo*pentanone (5·01 g.) and *n*-butylamine (4·30 g.), in methanol (20 ml.) containing concentrated hydrochloric acid (0·03 ml.), were hydrogenated in the presence of platinic oxide (94 mg.). After catalyst and solvent had been removed, the residue was distilled and furnished N-n-*butyl*cyclo*pentylamine* (IX) (7·52 g.), b. p. 186°, n_D^{23} 1·4460 (Found: C, 76·5; H, 12·9; N, 9·8. $C_9H_{19}N$ requires C, 76·5; H, 13·6; N, 9·9%), which gave a blue colour with nitroprusside–acetaldehyde reagent, and had characteristic absorption at 1136 cm.$^{-1}$. The derived *phenylurea* formed needles, m. p. 122°, from aqueous methanol (Found: C, 73·5; H, 8·8; N, 10·4. $C_{16}H_{24}ON_2$ requires C, 73·8; H, 9·3; N, 10·8%).

N-cyclo*Pentylidene*-n-*butylamine*.—(a) *Acid-catalysed liquid-phase synthesis.* When concentrated hydrochloric acid (0·6 ml.) was added to freshly distilled *cyclo*pentanone (84 g.) and *n*-butylamine (73 g.), exothermal reaction occurred. The whole was kept for 80 hr. at 20°. Ether (200 ml.) was added, and the solution was extracted with 2N-sulphuric acid (3 × 100 ml.). The basic product, liberated from these washings with alkali and isolated with ether (5 × 75 ml.), was kept at 25°/22 mm. for 30 min. and then distilled. N-cyclo*Pentylidene*-n-*butylamine* thus obtained (38·3 g.) had b. p. 91—92°/22 mm., n_D^{22} 1·4600 (Found: C, 77·8; H, 12·2; N, 10·3. $C_9H_{17}N$ requires C, 77·6; H, 12·3; N, 10·1%). It resisted hydrolysis with 2N-hydrochloric acid but yielded *cyclo*pentanone and *n*-butylamine when boiled with 5N-hydrochloric acid during 4 hr. Quantitative gas absorption occurred when *N-cyclo*pentylidene-*n*-butylamine (5·10 g.) in methanol (20 ml.) was hydrogenated over platinic oxide (100 mg.) with the formation of *N-n*-butyl*cyclo*pentylamine (IX) (4·51 g.), b. p. 186°, n_D^{22} 1·4468 (phenylurea, m. p. and mixed m. p. 122°).

(b) *Vapour-phase synthesis* (with I. Goodman). A mixture of *cyclo*pentanone (42 g.) and *n*-butylamine (36·5 g.) was dropped during 210 min. through a vertical glass tube (32 × 2 cm.) at 350°. Isolation from the dark-coloured, Ehrlich-negative, condensate by a procedure similar to that used in (*a*) gave *N-cyclo*pentylidene-*n*-butylamine (20·13 g.), b. p. 91—92°/22 mm.,

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n_D^{22} 1·4604 (Found: C, 77·0; H, 12·3; N, 10·2%) [hydrogenation gave N-*n*-butyl*cyclo*pentylamine, b. p. 186°, n_D^{22} 1·4468 (phenylurea derivative, m. p. and mixed m. p. 122°)].

N-n-*Butyl*-2-cyclo*pentyl*cyclo*pentylamine*.—Hydrogen (0·93 mol.) was absorbed when a solution of 2-*cyclo*pentyl*cyclo*pentanone (5·01 g.) and *n*-butylamine (2·31 g.) in methanol (20 ml.) containing concentrated hydrochloric acid (0·03 ml.) was hydrogenated over platinic oxide (95·5 mg.) during 20 hr. After catalyst and solvent had been removed, the residue, in ether (100 ml.), was shaken with 2N-hydrochloric acid (4 × 50 ml.). The basic product (5·20 g.), isolated by ether-extraction of the basified washings, was N-n-*butyl*-2-cyclo*pentyl*cyclo*pentyl-amine*, b. p. 78—80°/0·16 mm., n_D^{22} 1·4728 (Found: C, 80·8; H, 13·0; N, 6·6. $C_{14}H_{27}N$ requires C, 80·3; H, 13·0; N, 6·7%), which gave a blue colour with nitroprusside–acetaldehyde reagent. The derived *phenylurea* formed needles, m. p. 141°, from aqueous methanol (Found: C, 76·4; H, 9·7; N, 8·7. $C_{21}H_{32}ON_2$ requires C, 76·8; H, 9·8; N, 8·5%). The *α-naphthylthiourea*, m. p. 133° (Found: C, 76·3; H, 8·5; N, 6·6; S, 8·2. $C_{25}H_{34}N_2S$ requires C, 76·1; H, 8·7; N, 7·1; S, 8·1%), crystallised similarly.

N-n-*Butyl*-N-2-cyclo*pentyl*-α-cyclo*pentylacetamide*, prepared (1·3 g.) by boiling the foregoing base (1·57 g.) with acetic anhydride (1·5 ml.) and concentrated sulphuric acid (1 drop) for 30 min., had b. p. 130°/0·1 mm., n_D^{22} 1·4930 (Found: C, 76·8; H, 11·7; N, 6·1. $C_{16}H_{29}ON$ requires C, 76·4; H, 11·6; N, 5·6%), $\nu_{max.}$ 2900—2800s, 1650s, 1430s, 1367s, and 1295s cm.$^{-1}$.

N-(2-cyclo*Pentylidene*cyclo*pentylidene*)-n-*butylamine* (XX).—(*a*) No heat was evolved when concentrated hydrochloric acid (0·3 ml.) was added to 2-*cyclo*pentylidene*cyclo*pentanone (75 g.) and *n*-butylamine (36·5 g.). After 24 hr. at 20° the initial yellow colour had changed to red and after 5 days at 20° two layers had been formed. After 5 more days at 20°, ether (200 ml.) was added and the solution was shaken with 2N-sulphuric acid (4 × 100 ml.). Unchanged 2-*cyclo*pentylidene*cyclo*pentanone (22·4 g.) was recovered from the dried ethereal solution. The acid washings, when basified and extracted with ether, furnished *N*-(2-*cyclo*pentylidene*cyclo*pentylidene)-*n*-butylamine (XX), a deep yellow oil (57·6 g.), b. p. 92—94°/0·1 mm., n_D^{22} 1·5158, which, because of its rapid conversion into a red-brown resin, gave unsatisfactory analyses. When hydrolysed with boiling 5N-hydrochloric acid (20 ml.) for 8 hr., this base (1·02 g.) yielded 2-*cyclo*pentylidene*cyclo*pentanone (0·71 g.) [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 228—229° (decomp.)], and *n*-butylamine [picrate, m. p. and mixed m. p. 150—151°].

The base (5·03 g.) in methanol (20 ml.) was hydrogenated over platinic oxide (103 mg.), hydrogen (1·96 mol.) being absorbed. The basic product (4·16 g.) was *N*-*n*-butyl-2-*cyclo*pentyl*cyclo*-pentylamine, b. p. 77°/0·18 mm., n_D^{23} 1·4751 (Found: C, 80·2; H, 12·6; N, 6·9%), which gave a phenylurea, m. p. 140° (Found: C, 76·9; H, 9·6; N, 8·2%), and an α-naphthylthiourea, m. p. 133°, each identical with the authentic compounds.

(*b*) 2-*cyclo*Pentylidene*cyclo*pentanone (50 g.) and *n*-butylamine (24·3 g.) were mixed and dropped during 6 hr. through a vertical glass tube (32 cm. × 2 cm.) at 400°. The condensate, a brown oil, which contained globules of water and gave no colour with Ehrlich's reagent, was diluted with ether (200 ml.) and separated with dilute acid into basic and non-basic components, the latter being unchanged 2-*cyclo*pentylidene*cyclo*pentanone (35·83 g.). After removal of excess of *n*-butylamine at 20°/20 mm., the basic products were distilled and gave: (1) (trace) b. p. 70—82°/0·1 mm., n_D^{22} 1·4778; (2) (5·71 g.) b. p. 86—100°/0·1 mm., n_D^{22} 1·5005. Fraction (2) was mainly N-(2-cyclo*pentylidene*cyclo*pentylidene*)-n-*butylamine*, b. p. 88—92°/0·2 mm., n_D^{22} 1·5123, which rapidly resinified (Found: C, 81·0; H, 11·1; N, 5·0. $C_{14}H_{23}N$ requires C, 81·9; H, 11·3; N, 6·8%). Similar results were observed when a tube packed with glass balls (0·40 cm. diam.) was used to increase contact time.

Hydrogenation of the foregoing Schiff's base (1·095 g.) in methanol (20 ml.) over platinic oxide (56·5 mg.) afforded *N*-*n*-butyl-2-*cyclo*pentyl*cyclo*pentylamine (0·67 g.), b. p. 104—106°/1·6 mm., n_D^{21} 1·4760 (phenylurea, m. p. and mixed m. p. 137°).

High-temperature Reaction of cyclo*Pentanone and Related Compounds with Aliphatic Bases in the Vapour Phase over Activated Alumina: General Procedure*.—The appropriate ketones and bases were mixed together at room temperature and dropped down a vertical glass tube (32 cm. × 2 cm. diam.) packed with activated alumina (4—8 mesh), at ~350° (cf. Table 2). The products condensed at the bottom of the reaction chamber, generally as dark viscous oils containing globules of water, which gave intense purple colours with Ehrlich's reagent. Usually a strong odour of amine and hydrocarbon was associated with these products, which were separated into basic and non-basic components with ether and 2N-sulphuric acid in the usual way. The dried extracts of these materials were evaporated, and each was examined in detail.

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Reaction of 2-cyclo*Pentylidene*cyclo*pentanone with* n-*Butylamine in Vapour Phase at* 360° *over Activated Alumina* (Table 2, Expt. 1).—(a) *Basic products.* This material distilled as a yellow oil (11·55 g.), b. p. 30—140°/0·05 mm., n_D^{23} 1·5029, and when hydrogenated in methanol solution (20 ml.) over platinic oxide (100 mg.) absorbed hydrogen (1016 ml. at N.T.P.) equivalent to the presence of 4·65 g. of the Schiff's base (XX). Distillation of the hydrogenated

TABLE 2. *High-temperature reactions of* cyclo*pentanone and related compounds with aliphatic amines in the vapour phase over activated alumina.*

Expt.	Reactants: Ketone, g. (mole)	Base, g. (mole)	Temp.	Reaction period (min.)
1	2-*cyclo*Pentylidene*cyclo*pentanone 75 (0·50)	NH_2Bu 36·5 (0·50)	360° ± 5°	270
2	2-*cyclo*Pentylidene*cyclo*pentanone 47·2 (0·315)	Schiff's base (XX) 32·18 (0·157	350 ± 10 (in N_2)	—
3	2-Butylidene*cyclo*pentanone 33·3 (0·241)	Schiff's base (XIX) 24·7 (0·121)	—	180
4	*cyclo*Pentanone 84 (1·0)	NH_2Bu 73 (1·0)	350 ± 5	—

bases afforded: (1) (trace) b. p. 40—70°/0·01 mm.; (2) (4·23 g.) b. p. 70—90°/0·01 mm., n_D^{22} 1·4811; (3) (5·0 g.) b. p. 90—124°/0·01 mm., n_D^{23} 1·5078. After recombination, fractions (2) and (3) were treated with acetic anhydride (10 ml.) and concentrated sulphuric acid (2 drops) at 100° for 30 min., and the mixture then cooled and added to water (200 ml.). Two hours later, excess of 2N-sodium hydroxide was added and the product, after isolation with ether (5 × 75 ml.), was separated into acetylated and non-acetylated bases with 2N-sulphuric acid (4 × 75 ml.) in the usual way. Distillation of the tertiary basic material yielded 6-*n*-propyl-2 : 3·4 : 5-di*cyclo*pentenopyridine (III; R = Pr^n) (3·54 g., 0·0176 mole), b. p. 104—106°/0·08 mm., n_D^{22} 1·5370 (Found: C, 83·7; H, 9·7; N, 6·8. Calc. for $C_{14}H_{19}N$: C, 83·5; H, 9·5; N, 7·0%), having the light and infrared absorption described by Goodman [2,31] who gives b. p. 104—106°/0·6 mm., n_D^{21} 1·5405. The mass spectrum confirmed the main constituent as the tertiary base (III; R = Pr^n); weak peaks at mass : charge ratios 215 (III; R = Bu^n), 173 (III; R = Me), 159 (III; R = H), 207 (VIII; R = H, R′ = Pr^n), and at 186, 147, and 146 (unidentified), were also present. The chloroplatinate, orange needles from chloroform–light petroleum (b. p. 60—80°), had, after desolvation at 100°/0·1 mm. for 6 hr., m. p. and mixed m. p. 187° (decomp.), and gave an *X*-ray powder photograph identical with that from the authentic chloroplatinate [Found: C, 41·7; H, 4·8; N, 3·6; Cl, 27·2; Pt(ash), 24·0. Calc. for $C_{28}H_{40}N_2Cl_6Pt$: C, 41·4; H, 5·0; N, 3·45; Cl, 26·2; Pt, 24·0%].

The acetylated hydrogenated bases were mainly *N*-*n*-butyl-*N*-(2-*cyclo*pentyl*cyclo*pentyl)-acetamide (5·65 g.), b. p. 106—114°/0·07 mm., n_D^{22} 1·4891 (Found: C, 76·5; H, 11·8; N, 5·8. Calc. for $C_{16}H_{29}ON$: C, 76·4; H, 11·6; N, 5·6%) (infrared spectrum).

From a second experiment, the hydrogenated basic material [corresponding to fractions (2) and (3) above] (2·0 g.) was warmed with phenyl *iso*cyanate (1·0 g.) in light petroleum (b. p. 60—80°; 15 ml.) for 10 min., then kept at 20° for 4 hr.; the mixture deposited *N*-*n*-butyl-2-*cyclo*pentyl*cyclo*pentyl-*N*′-phenylurea, m. p. and mixed m. p. 141° (Found: C, 76·7; H, 9·8; N, 8·6, 8·4. Calc. for $C_{21}H_{32}ON_2$: C, 76·8; H, 9·8; N, 8·5%).

(b) *Non-basic products.* This material, when distilled, gave: (4) (15·70 g.) b. p. 106—128°/17 mm.; (5) (14·08 g.) b. p. 54—128°/0·07 mm.; a viscous involatile residue (4·82 g.) remained. Infrared spectra indicated the major components of these fractions to be 2-*cyclo*pentyl*cyclo*pentanone [38% in (4); 17% in (5)] and 2-*cyclo*pentylidene*cyclo*pentanone [19% in (4); 31% in (5)]. Since, however, other unidentified *cyclo*pentanone derivatives with absorption bands overlapping those due to these two ketones were also probably present, analysis by infrared measurement was not accurate. The foregoing figures were arrived at by measurement of the bands at 1275 cm.$^{-1}$ in the spectrum of 2-*cyclo*pentyl*cyclo*pentanone and at 895 cm.$^{-1}$ in that of 2-*cyclo*pentylidene*cyclo*pentanone, and indicated the formation of a total of 8·48 g. (0·0558 mole) of 2-*cyclo*pentyl*cyclo*pentanone in the reaction. The molecular ratio of 2-*cyclo*pentyl*cyclo*pentanone to base (III; R = Pr^n) produced in the condensation was therefore 0·0558 : 0·0176 (3·17 : 1).

After filtration through activated alumina, a chloroform solution of the 2 : 4-dinitrophenylhydrazone (0·95 g.) from fraction (4) (0·80 g.) was evaporated and the residue was crystallised

[31] Dr. I. Goodman, personal communication.

from ethyl acetate. Repeated crystallisation (from ethyl acetate) of the dark red crystals which were deposited gave 2-*cyclo*pentylidene*cyclo*pentanone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 228—229° (decomp.). The residue left after evaporation of the mother-liquors from the original crystallisation was repeatedly crystallised from methanol and yielded 2-*cyclo*pentyl*cyclo*pentanone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 154—155°. The mixed semicarbazones (1·17 g.) from fraction (4) (2·0 g.) furnished the semicarbazone of 2-*cyclo*pentyl*cyclo*pentanone, m. p. and mixed m. p. 202°; no pure sample of 2-*cyclo*pentylidene-*cyclo*pentanone semicarbazone was isolated from the mother-liquors.

The 2 : 4-dinitrophenylhydrazone (1·03 g.) from fraction (5) (1·00 g.) was filtered in chloroform through activated alumina, and when then repeatedly recrystallised from ethyl acetate gave 2-*cyclo*pentylidene*cyclo*pentanone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229° (decomp.). When evaporated, the original mother-liquor yielded a red gum from which no further crystalline derivatives were isolated.

Reaction of 2-cyclo*Pentylidene*cyclo*pentanone with* N-(2-cyclo*Pentylidene*cyclo*pentylidene*)-n-*butylamine in the Vapour Phase at* 350° *over Activated Alumina* (Table 2, Expt. 2).—(a) *Basic products.* From this material (6·94 g.), after unchanged Schiff's base had been removed by hydrogenation and subsequent acetylation, the pyridine derivative (III; R = Pr^n) (3·22 g., 0·0162 mole), b. p. 92—98°/0·07 mm., n_D^{22} 1·5395 (Found: C, 83·1; H, 9·8; N, 7·3%) (light and infrared spectra), was isolated. The mass spectrum had a major peak at mass : charge ratio 201, and smaller peaks at 229 (III; R = *n*-C_5H_{11}), 215 (III; R = Bu^n), 173 (III; R = Me), and 159 (III; R = H), and at 207, 186, and 164 [all derived from the hydrogenated base (VIII; R = H, R′ = Pr^n)]. The chloroplatinate, after desolvation at 100°/0·1 mm. during 8 hr., had m. p. and mixed m. p. 188° (decomp.) and gave an *X*-ray powder photograph identical with that from authentic salt [Found: C, 41·8; H, 4·1; N, 3·4; Cl, 26·8; Pt(ash), 22·0%].

(b) *Non-basic products.* This material furnished: (1) (10·04 g.) b. p. 60—140°/14 mm.; (2) (8·26 g.) b. p. 90—140°/0·1 mm. Infrared absorption measurements indicated the major components of these fractions to be 2-*cyclo*pentylidene*cyclo*pentanone [45% in (1); 20% in (2)] and 2-*cyclo*pentyl*cyclo*pentanone [45% in (1); 30% in (2)]. From fraction (1), 2-*cyclo*pentyl-*cyclo*pentanone was isolated as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 159°, and the semicarbazone, m. p. and mixed m. p. 207—208°, whilst 2-*cyclo*pentylidene*cyclo*-pentanone was obtained as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 228° (decomp.) from both (1) and (2). The total amount of 2-*cyclo*pentyl*cyclo*pentanone from (1) and (2) (from infrared measurements) amounted to 6·17 g. (0·0406 mole); thus the molecular ratio of 2-*cyclo*pentyl*cyclo*pentanone to pyridine (III; R = Pr^n) produced in the reaction was 0·0406 : 0·0162 (2·52 : 1).

2-n-*Butyl*cyclo*pentanone and* 2 : 5-*Di*-n-*butyl*cyclo*pentanone.*—Freshly distilled, acid-free *n*-butyraldehyde (144 g., 2 moles) was added during 6 hr. to a stirred mixture of *cyclo*pentanone (168 g., 2 moles), ether (80 ml.), and 12% aqueous sodium hydroxide (200 ml.) at 10—20°. 60 Min. later the brown, heterogeneous oil was diluted with water (300 ml.), and the whole was made slightly acid (Congo Red) with concentrated hydrochloric acid, and extracted with ether (4 × 200 ml.). The residue (combined material from 4 similar experiments) remaining after evaporation of the dried, ethereal solution was distilled and gave: (1) (158·8 g.) b. p. 30—70°/12 mm.; (2) (618·5 g.) b. p. 90—133°/12 mm.; (3) (81 g.) b. p. 133—160°/12 mm. Fraction (1) was unchanged *cyclo*pentanone. Fraction (2) was boiled under reduced pressure (45 mm.) with anhydrous oxalic acid, and after water (65 ml.) had been removed azeotropically (Dean–Stark), was distilled and furnished a pale yellow oil (515 g.) which upon repeated distillation yielded 2-*butylidene*cyclo*pentanone* (XVIII), b. p. 90°/12 mm., n_D^{22} 1·4815 (Found: C, 78·4; H, 10·1. $C_9H_{14}O$ requires C, 78·2; H, 10·2%), $\lambda_{max.}$ (in MeOH) 245 mμ (log ε 4·03). The C=O absorption band was at 1724—1709s cm.$^{-1}$. The 2 : 4-*dinitrophenylhydrazone* separated from ethyl acetate in deep red needles, m. p. 163—164° (Found: C, 57·1; H, 6·1; N, 17·4. $C_{15}H_{18}O_4N_4$ requires C, 56·6; H, 5·7; N, 17·6%). The *semicarbazone*, needles from aqueous methanol, had m. p. 204° (Found: C, 61·8; H, 8·4; N, 20·9. $C_{10}H_{17}ON_3$ requires C, 61·45; H, 8·8; N, 21·5%).

Hydrogenation of 2-butylidene*cyclo*pentanone (10·2 g.) in methanol (150 ml.) over Raney nickel (1·0 g.) afforded 2-*n*-butyl*cyclo*pentanone, b. p. 86°/15 mm., n_D^{22} 1·4448 (Found: C, 77·1; H, 11·2. Calc. for $C_9H_{16}O$: C, 77·1; H, 11·5%) (Rapson and Shuttleworth [32] record b. p.

[32] Rapson and Shuttleworth, *J.*, 1940, 640.

89°/10 mm., n_D^{20} 1·4568). The C=O absorption was at 1727 cm.$^{-1}$. The 2 : 4-*dinitrophenylhydrazone* of this ketone separated from methanol in yellow-orange needles, m. p. 110—111° (Found: C, 56·8; H, 6·2; N, 17·4. $C_{18}H_{26}O_4N_4$ requires C, 56·2; H, 6·3; N, 17·6%). The semicarbazone formed rosettes of small prismatic needles, m. p. 197°, from methanol (Found: C, 60·7; H, 9·7; N, 21·2. Calc. for $C_{16}H_{19}ON_3$: C, 60·9; H, 9·7; N, 21·3%) (Rapson and Shuttleworth [32] give m. p. 185—186°; Goodman [2,31] found m. p. 188—189°).

Fraction (3) (147·9 g.) and anhydrous oxalic acid (3·0 g.) were boiled under reflux at 42 mm. and liberated water was removed (Dean–Stark). After being washed with 2N-sodium hydrogen carbonate and dried (Na_2SO_4), an ethereal solution of the residue was evaporated and distilled to give: (4) (26·78 g.) b. p. 104—123°/18 mm.; (5) (17·40 g.) b. p. 123—140°/18 mm.; (6) (65·58 g.) b. p. 140—186°/18 mm.; a high-boiling residue (23·0 g.) remained. From fraction (6), two further fractions, (7) (7·95 g.) b. p. 60—80°/0·07 mm., n_D^{24} 1·4917, and (8) (53·20 g.) b. p. 80—82°/0·08 mm., n_D^{24} 1·4980, were obtained. Repeated distillation of sub-fraction (8) gave 2 : 5-*dibutylidene*cyclo*pentanone* as a lemon-yellow oil (45·0 g.), b. p. 80°/0·08 mm., n_D^{24} 1·4971 (Found: C, 81·1; H, 10·3. $C_{18}H_{30}O$ requires C, 81·2; H, 10·5%), $\lambda_{max.}$ 251 mμ (log ε 3·94) (in MeOH). The C=O absorption was at 1684 cm.$^{-1}$.

Hydrogenation of 2 : 5-dibutylidene*cyclo*pentanone (10·16 g.) in methanol (150 ml.) over Raney nickel (1·0 g.) afforded 2 : 5-di-*n*-butyl*cyclo*pentanone, a colourless oil (8·45 g.), b. p. 140—141°/20 mm., n_D^{22} 1·4497 (Found: C, 79·5; H, 11·9. Calc. for $C_{13}H_{24}O$: C, 79·5; H, 12·3%) (Goodman [2,31] found b. p. 140—142°/13 mm., n_D^{26} 1·4495). The C=O absorption was at 1718 cm.$^{-1}$. The semicarbazone separated from aqueous methanol as needles, m. p. 116° (Found: C, 66·5; H, 10·6; N, 16·8. Calc. for $C_{14}H_{27}ON_3$: C, 66·4; H, 10·7; N, 16·6%) (Goodman [2,31] found m. p. 116—117°). The 2 : 4-*dinitrophenylhydrazone* formed orange needles, m. p. 62—63° (from much methanol) (Found: C, 60·6; H, 7·6; N, 14·3. $C_{19}H_{28}O_4N_4$ requires C, 60·6; H, 7·5; N, 14·9%).

2-n-*Butyldi*cyclo*pentylamine*.—Hydrogen (1·03 mol.) was absorbed when 2-*n*-butyl*cyclo*pentanone (5·0 g.) and *cyclo*pentylamine (3·1 g.) in methanol (20 ml.) containing concentrated hydrochloric acid (0·03 ml.) were reduced over platinic oxide (1·0 g.) during 48 hr. Isolated in the usual manner, 2-n-*butyldi*cyclo*pentylamine* was obtained as a colourless oil (5·50 g.), b. p. 78°/0·2 mm., n_D^{22} 1·4730 (Found: C, 79·7; H, 13·0; N, 6·4. $C_{14}H_{27}N$ requires C, 80·3; H, 13·0; N, 6·7%). This base did *not* give a colour reaction with nitroprusside–acetaldehyde reagent, and had infrared bands at 1176ms, 1149ms, and 1124ms cm.$^{-1}$. The *phenylurea* formed needles, m. p. 127—128°, from aqueous methanol (Found: C, 76·2; H, 9·8; N, 8·5. $C_{21}H_{32}ON_2$ requires C, 76·8; H, 9·8; N, 8·5%).

N-(2-*Butylidene*cyclo*pentylidene*)cyclo*pentylamine* (XIX).—A mixture of 2-butylidene*cyclo*pentanone (81 g.) and *cyclo*pentylamine (50 g.) was treated with concentrated hydrochloric acid (2 ml.) and kept at 20°. After 15 hr., two layers had formed and after 6 days the heterogeneous product was diluted with ether (300 ml.) and separated by the usual procedure into basic and non-basic components; of these, the latter was unchanged 2-butylidene*cyclo*pentanone (31·5 g.). The basic material afforded *N*-(2-butylidene*cyclo*pentylidene)*cyclo*pentylamine (XIX), a yellow oil (26·7 g.), b. p. 86—123°/0·3 mm., n_D^{25} 1·5098, which rapidly resinified; much decomposition attended the distillation and a considerable residue remained. When boiled under reflux with 5N-hydrochloric acid (20 ml.) during 20 hr., this Schiff's base (1·05 g.) yielded 2-butylidene*cyclo*pentanone (0·65 g.) (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 162°) and *cyclo*pentylamine (identified by paper chromatography).

Hydrogenation of this product (XIX) (2·04 g.) in methanol (20 ml.) over platinic oxide (300 mg.) gave 2-*n*-butyldi*cyclo*pentylamine (1·36 g.), b. p. 80—81°/0·3 mm., n_D^{25} 1·4744 (Found: C, 80·2; H, 12·8; N, 6·8%) (infrared spectrum; phenylurea, m. p. and mixed m. p. 127°).

4-n-*Propyl*-2 : 3·5 : 6-*di*cyclo*pentenopyridine* (XVII).—(a) *From* 2-*butylidene*cyclo*pentanone and* cyclo*pentylamine*. *cyclo*Pentylamine (35 g., 0·415 mole), 2-butylidene*cyclo*pentanone (170·5 g., 1·235 moles), and ammonium acetate crystals (10 g.) were heated together at 200° ± 5° under autogenous pressure (max. was 175 lb./sq. in.) during 10 hr. After being cooled the product, a dark, Ehrlich-positive, mobile oil was separated with ether and N-sulphuric acid into non-basic and basic constituents.

(i) *Non-basic products*. This material was distilled and gave: (1) (9·05 g.) b. p. 40—80°/17 mm., n_D^{22} 1·4336; (2) (20·30 g.) b. p. 80—90°/15 mm., n_D^{22} 1·4447; (3) (15·11 g.) b. p. 96—140°/15 mm., n_D^{22} 1·4700; (4) (3·27 g.) b. p. 140—145°/15 mm. to 80—100°/0·2 mm., n_D^{22} 1·4791; (5) (2·24 g.) b. p. 100—117°/0·2 mm., n_D^{22} 1·4935. Fraction (1) was mainly *cyclo*pentanone

[2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 144°; semicarbazone, m. p. and mixed m. p. 217—218° (decomp.)]. Fraction (2) was essentially 2-*n*-butyl*cyclo*pentanone (semicarbazone, m. p. and mixed m. p. 197°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 112—113°). Fraction (3) had as principal components 2 : 5-di-*n*-butyl*cyclo*pentanone and 2-*cyclo*pentylidene*cyclo*pentanone (light and mass spectra). The mass spectrum of fraction (5) showed parent peaks at the following mass : charge ratios: 262 (a dibutyl*cyclo*pentylidene*cyclo*pentanone ?), 206 (*x*-butylidene-2-*cyclo*pentyl*cyclo*pentanone ?), and 150 (2-*cyclo*pentylidene-*cyclo*pentanone).

(ii) *Basic products.* Distillation of the crude basic products (68·1 g.) yielded: (6) (7·85 g.) b. p. 88—104°/0·2 mm., n_D^{22} 1·5134; (7) (3·50 g.) b. p. 104—110°/0·2 mm., n_D^{22} 1·5410; (8) (22·64 g.) b. p. 110—117°/0·35 mm., n_D^{22} 1·5440; (9) (10·76 g.) b. p. 117—138°/0·35 mm., n_D^{22} 1·5531. Fractions (7) and (8) were recombined and heated at 100° for 2 hr. with acetic anhydride (25 ml.) and concentrated sulphuric acid (4 drops). The cooled mixture was poured into water (800 ml.) and separated into acetylated and non-acetylated bases by the usual procedure. When distilled, the non-acetylated bases furnished fractions, (10) (13·48 g.) b. p. 106—120°/0·3 mm., n_D^{20} 1·5434, and (11) (9·62 g.) b. p. 120—140°/0·3 mm., n_D^{20} 1·5429. Fraction (10) on further distillation yielded two sub-fractions: (12) (9·53 g.) colourless, b. p. 106—112°/0·3 mm., $n_D^{21·5}$ 1·5429; (13) (3·01 g.) pale yellow, b. p. 112—120°/0·3 mm., $n_D^{21·5}$ 1·5413; the former was 4-n-*propyl*-2 : 3-5 : 6-*di*cyclo*pentenopyridine* (XVII) (Found: C, 84·0; H, 9·5; N, 7·0. $C_{14}H_{19}N$ requires C, 83·5; H, 9·5; N, 7·0%); $\lambda_{max.}$ 282 mμ (log ε 3·89), $\lambda_{min.}$ 237 mμ (log ε 2·83) in MeOH; $\lambda_{max.}$ 232, 291 mμ (log ε 3·62, 4·04), $\lambda_{infl.}$ 237 mμ (log ε 3·56), $\lambda_{min.}$ 251 mμ (log ε 2·44) in conc. HCl; $\nu_{max.}$ 1592s (pyridine ring), and 2976—2874s, 1468s, 1437s, and 1391s cm.$^{-1}$ (CH_2 and Me). The mass spectrum contained a parent peak at mass : charge ratio 201 and was closely similar to that given by the isomeric pyridine (III; R = Pr^n). The *chloroplatinate*, orange needles [from chloroform–light petroleum (b. p. 60—80°)], after drying at 80°/0·2 mm. for 8 hr., had m. p. 192° (decomp.) [Found: C, 42·0; H, 4·7; N, 3·5; Cl, 27·0; Pt(ash), 23·2. $C_{28}H_{40}N_2Cl_6Pt$ requires C, 41·4; H, 5·0; N, 3·45; Cl, 26·2; Pt, 24·0%].

When reduced with sodium metal (10 g.) in boiling ethanol (60 ml.), the pyridine (XVII) (2·14 g.) afforded 4-n-*propyl*-2 : 3-5 : 6-*di*cyclo*pentanopiperidine* (1·84 g.), b. p. 96—98°/0·4 mm., n_D^{24} 1·5020 (Found: C, 81·3; H, 12·3; N, 6·8. $C_{14}H_{25}N$ requires C, 81·1; H, 12·15; N, 6·8%), which gave a blue colour with nitroprusside–acetaldehyde reagent. Light absorption was not significant at wavelengths greater than 230 mμ. Infrared bands were at 1134ms (ring –NH–) and 2959—2841s, 1449s, and 1379ms cm.$^{-1}$ (CH_2 and Me).

A suspension of 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine (4·28 g.) in water (500 ml.) was treated at room temperature with potassium permanganate (30 g.) during 48 hr., then worked up as for analogous material derived from the base (III; R = Bu^n). Paper-chromatography of the volatile acids (0·35 g.) indicated butyric, propionic, and acetic acid. The non-volatile acids, a yellow gum (3·84 g.) which gave a yellow-orange colour with aqueous ferrous sulphate, had light absorption max. at 279 and min. at 261 mμ in MeOH.

(b) *From* 2-*butylidene*cyclo*pentanone* (XVIII) *and* N-(2-*butylidene*cyclo*pentylidene*)cyclo*pentylamine* (XIX) *in the vapour phase at* 350° *over activated alumina* (Table 2, Expt. 3). (i) Unchanged base (XIX) was removed from the basic products (7·80 g.), b. p. 92°/0·3 mm. to 160°/0·4 mm., by hydrogenation and subsequent acetylation, and the residual tertiary bases were distilled. Of the 3 fractions obtained, *viz.*, (1) (0·61 g.) b. p. 102—110°/0·22 mm., n_D^{22} 1·5395, (2) (3·52 g.) b. p. 112—125°/0·22 mm., n_D^{22} 1·5380, and (3) (1·12 g.) b. p. 125—163°/0·22 mm., n_D^{22} 1·5320, fractions (1) and (2) were recombined and redistilled to yield two further fractions: (4) (2·93 g.) b. p. 110—120°/0·3 mm. and (5) (1·20 g.) b. p. >120°/0·3 mm. Fraction (4) was mainly 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine, b. p. 112—118°/0·5 mm., n_D^{22} 1·5386 (Found: C, 84·1; H, 9·4; N, 7·2%), having ultraviolet and infrared absorption spectra identical with those of the base synthesised by route (a). The mass spectrum was closely similar to that of the latter material; additional weak peaks at mass : charge ratios 229, 215, 147, 146, and 159 were present. The chloroplatinate, after drying at 80°/0·15 mm. for 8 hr., had m. p. and mixed m. p. 183° (decomp.) [Found: C, 42·0; H, 5·1; N, 3·6; Cl, 26·4; Pt(ash), 23·0%] and gave an *X*-ray powder photograph identical with that of the derivative synthesised by route (a).

(ii) Distillation of the non-basic products afforded fractions (6) (10·87 g.) b. p. 65—125°/25 mm., n_D^{20} 1·4559, and (7) (13·84 g.) b. p. 83—162°/0·5 mm., n_D^{22} 1·4945; a viscous residue (8·43 g.) remained. The infrared spectra indicated the presence, in each, of both saturated and

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unsaturated *cyclo*pentanone derivatives. Fraction (6) was largely 2-*n*-butyl*cyclo*pentanone (semicarbazone, m. p. and mixed m. p. 194°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 110—111°).

Reaction of cyclo*Pentanone with* n-*Butylamine at* 300° (Table 1; Expt. 4).—(a) *Non-basic products.* Distillation of this component afforded: (1) (1·91 g.) b. p. 65—72°/0·5 mm., n_D^{22} 1·4562; (2) (20·10 g.) b. p. 78—85°/0·5 mm., n_D^{22} 1·4529; (3) (11·67 g.) b. p. 85—93°/0·3 mm., n_D^{22} 1·4611; (4) (22·12 g.) b. p. 93—103°/0·15 mm., n_D^{22} 1·4830; (5) (10·46 g.) b. p. 103—180°/0·15 mm., n_D^{22} 1·4911; a viscous residue (12·06 g.) was left. All these materials rapidly darkened on exposure to air and light, and contained traces of nitrogenous compounds.

Fraction (1) was mainly 2-*n*-butyl*cyclo*pentanone (semicarbazone, m. p. and mixed m. p. 190°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 110°). Fraction (2) was primarily 2 : 5-di-*n*-butyl*cyclo*pentanone with smaller amounts of other saturated *cyclo*pentanone compounds (infrared spectrum). This fraction (4·0 g.) yielded 2 : 5-di-*n*-butyl*cyclo*pentanone semicarbazone (4·5 g.), m. p. and mixed m. p. 122° (Found: C, 66·5; H, 10·5; N, 16·8. Calc. for $C_{14}H_{27}ON_3$: C, 66·4; H, 10·7; N, 16·6%). After being boiled with ethanolic 2 : 4-dinitrophenylhydrazine hydrochloride fraction (2) (1·0 g.) deposited, on cooling, a red gum which was dissolved in chloroform and filtered through activated alumina. The solvent was evaporated, the residue was dissolved in methanol; and the bright red prisms (55 mg.) which were deposited after the solution had been kept at 20° for 14 days were collected and recrystallised from methanol. This 2 : 4-*dinitrophenylhydrazone* (Found: C, 61·0; H, 7·6; N, 13·2%) had m. p. 71—72° which was depressed upon admixture with 2 : 5-di-*n*-butyl*cyclo*pentanone 2 : 4-dinitrophenylhydrazone; these two derivatives also gave different *X*-ray diffraction patterns.

Fraction (3) contained less 2 : 5-di-*n*-butyl*cyclo*pentanone and more of the other *cyclo*pentanone compounds than fraction (2) (infrared spectrum). This fraction (2·0 g.) yielded 2 : 5-di-*n*-butyl*cyclo*pentanone semicarbazone (1·55 g.), m. p. and mixed m. p. 116°; a crystalline 2 : 4-dinitrophenylhydrazone was not isolated.

The infrared spectra of fractions (4) and (5) were very similar and indicated the presence of both saturated and unsaturated *cyclo*pentanone compounds.

(b) *Basic products.* When distilled, this component gave fractions: (6) (1·20 g.) b. p. 76—80°/25 mm., n_D^{22} 1·4232; (7) (2·79 g.) b. p. 80—104°/0·1 mm., n_D^{22} 1·4832; (8) (10·01 g.) b. p. 104—114°/0·2 mm., n_D^{22} 1·5214; (9) (14·54 g.) b. p. 114—158°/0·2 mm., n_D^{22} 1·5309; (10) (1·54 g.) b. p. 158—200°/0·25 mm., n_D^{22} 1·5350; an involatile pitch (2·04 g.) remained.

Fraction (6) contained dibutylamine (picrate, m. p. and mixed m. p. 58°). Fraction (7) was a complex mixture containing *cyclo*pentanone derivatives (infrared spectrum), amide, and pyridine bases (as (XVII). Fractions (8) and (9) contained as principal constituent the base (XVII) (spectra).

The total crude basic material (46·5 g.) from a second similar reaction was stirred with 10% aqueous sodium hydroxide (1 l.), and benzenesulphonyl chloride (75 ml.) was added during 2 hr. Next day, the mixture was heated at 70° for 2 hr., then extracted with ether (8 × 100 ml.). From this extract, the tertiary bases were isolated with 2N-sulphuric acid in the usual way and were obtained as a yellow oil, essentially 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine (7·51 g.), b. p. 104—108°/0·25 mm., n_D^{22} 1·5376 (Found: C, 83·6; H, 9·9; N, 6·7%) [light, infrared, and mass spectra; chloroplatinate, m. p. and mixed m. p. 187° (decomp.); behaviour on oxidation].

Reaction of cyclo*Pentanone with* n-*Butylamine in the Vapour Phase at* 350° *over Activated Alumina* (Table 2, Expt. 4).—(a) *Basic products.* Distillation of the crude bases yielded fractions: (1) (10·06 g.) b. p. 96—104°/32 mm., n_D^{22} 1·4569; (2) (3·30 g.) b. p. 104—128°/32 mm., n_D^{22} 1·4625; (3) (1·22 g.) b. p. 42—70°/0·04 mm., n_D^{22} 1·4639; (4) (16·34 g.) b. p. 70—130°/0·04 mm. n_D^{22} 1·5019. Of these, only fractions (1) and (4) were examined.

Fraction (1) was *N-cyclo*pentylidene-*n*-butylamine, and when hydrogenated over platinum oxide quantitatively absorbed hydrogen to yield *N-n*-butyl*cyclo*pentylamine (phenylurea, m. p. and mixed m. p. 122°). When fraction (4) (16·34 g.) in methanol (40 ml.) was hydrogenated over platinic oxide (500 mg.), hydrogen uptake (1321 ml. at N.T.P.) equivalent to the presence of 6·05 g. of *N*-(2-*cyclo*pentylidene*cyclo*pentylidene)-*n*-butylamine took place. The hydrogenation product (13·3 g.), b. p. 40—130°/0·2 mm., n_D^{22} 1·4929, which gave a blue colour with nitroprusside–aldehyde reagent, was treated with acetic anhydride (15 ml.) containing concentrated sulphuric acid (2 drops) at 100° during 30 min., and then separated into acetylated and non-acetylated components. The acetylated bases contained *N-n*-butyl-*N*-2-*cyclo*pentyl*cyclo*pentylacetamide (4·35 g.), b. p. 115—122°/0·35 mm., n_D^{22} 1·4820 (Found: C, 74·5; H, 11·8; N,

7·3. Calc. for $C_{16}H_{29}ON$: C, 76·4; H, 11·6; N, 5·6%) (infrared spectrum). The non-acetylated basic product was 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine (4·0 g.), b. p. 98—106°/0·08 mm., n_D^{22} 1·5367 (Found: C, 83·5; H, 9·6; N, 7·1%) [light, infrared, and mass spectra; chloroplatinate, m. p. and mixed m. p. 186° (decomp.)].

(b) *Non-basic products.* The crude non-basic products (32·4 g.) were distilled and gave six Ehrlich-positive fractions, all of which rapidly darkened upon exposure to air and light: (5) (0·87 g.) b. p. 32—76°/19 mm., n_D^{22} 1·4284; (6) (2·44 g.) b. p. 80—108°/19 mm., n_D^{22} 1·4848; (7) (3·00 g.) b. p. 52—106°/0·1 mm., n_D^{22} 1·4926; (8) (1·05 g.) b. p. 62—84°/0·06 mm., n_D^{22} 1·4957; (9) (5·60 g.) b. p. 84—96°/0·06 mm., n_D^{22} 1·5085; (10) (2·30 g.) b. p. 96—128°/0·06 mm., n_D^{22} 1·5282. Fraction (5) was essentially unchanged *cyclo*pentanone. Infrared spectra showed the other fractions to be complex mixtures, whose principal components were 2-*cyclo*pentylidene- (total 2·09 g.) and 2-*cyclo*pentyl-*cyclo*pentanone (2·03 g.). The ratio of 2-*cyclo*pentyl*cyclo*pentanone to 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine produced was 0·67 : 1 molar.

Reaction of cyclo*Pentanone with Di*-n-*butylamine at* 300° (Table 1, Expt. 5).—(a) *Non-basic products.* Distillation of the crude, Ehrlich-positive, material yielded fractions: (1) (0·96 g.) b. p. up to 60°/15 mm., n_D^{22} 1·4333; (2) (9·89 g.) b. p. 88—96°/15 mm., n_D^{22} 1·4498; (3) (10·58 g.) b. p. 96—115°/15 mm., n_D^{22} 1·4697; (4) (2·79 g.) b. p. 62—88°/0·07 mm., n_D^{22} 1·4721; (5) (6·84 g.) b. p. 88—114°/0·1 mm., n_D^{22} 1·4760; (6) (12·00 g.) b. p. 114—180°/0·4 mm., n_D^{22} 1·5038; an involatile pitch (20·42 g.) remained.

Fraction (1) was unchanged *cyclo*pentanone. Fraction (2) was 2-*n*-butyl*cyclo*pentanone (infrared spectrum; semicarbazone, m. p. and mixed m. p. 197°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 110°). Fractions (3) and (4) each had as major component 2-*cyclo*pentyl-*cyclo*pentanone (semicarbazone, m. p. and mixed m. p. 202—203°; 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 153°), and minor component 2-*n*-butyl*cyclo*pentanone (mass spectrum). Infrared spectra indicated the presence in fractions (5) and (6) of saturated and unsaturated *cyclo*pentanones with the latter predominating.

(b) *Basic products.* Distillation of these products yielded fractions: (7) (86·76 g.) b. p. 160—162°/760 mm., n_D^{22} 1·4241; (8) (1·83 g.) b. p. 28—76°/0·1 mm., n_D^{22} 1·4558; (9) (5·76 g.) b. p. 76—102°/0·1 mm., n_D^{22} 1·5250; (10) (8·44 g.) b. p. 102—142°/0·1 mm., n_D^{22} 1·5378; a viscous residue (4·64 g.) remained.

Fraction (7) was unchanged di-*n*-butylamine. Fractions (9) and (10) were recombined and heated at 100° with acetic anhydride (15 ml.) and concentrated sulphuric acid (0·5 ml.) during 90 min. Only a trace of acetylated material was produced, whilst the non-acetylated bases were obtained as a colourless oil which was distilled to give materials, (11) (0·62 g.) b. p. 90—98°/0·3 mm., n_D^{22} 1·5210, and (12) (8·53 g.) b. p. 100—104°/0·3 mm., n_D^{22} 1·5415. The latter was largely 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine (7·50 g.), b. p. 100—102°/0·3 mm., n_D^{22} 1·5420 (Found: C, 83·2; H, 9·4; N, 7·0%) (light, infrared, and mass spectra; behaviour on oxidations).

Reaction of cyclo*Pentanone with Tri*-n-*butylamine at* 300° (Table 1, Expt. 6).—(a) *Non-basic products.* This material, which gave only a weak colour reaction with Ehrlich's reagent, was distilled to yield fractions: (1) (21·70 g.) b. p. 60°/65 mm., n_D^{22} 1·4350; (2) (19·70 g.) b. p. 140—150°/30 mm., n_D^{22} 1·5042; (3) (8·63 g.) b. p. 120—160°/0·2 mm., n_D^{22} 1·5289; a viscous residue (3·00 g.) remained.

Fraction (1) was unchanged *cyclo*pentanone. Fraction (2) was mainly 2-*cyclo*pentylidene-*cyclo*pentanone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229° (decomp.)]. The partly crystalline, yellow fraction (3) was a mixture containing the ketone (XI) (m. p. and mixed m. p. 79—80°) and 2-*cyclo*pentylidene*cyclo*pentanone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 229—230° (decomp.)].

(b) *Basic products.* When distilled, this material gave fractions: (4) (179·9 g.) b. p. 210—216°/760 mm., n_D^{22} 1·4296; (5) (0·39 g.) b. p. up to 100°/0·4 mm., n_D^{22} 1·4572; (6) (1·18 g.) b. p. 100—120°/0·4 mm., n_D^{22} 1·5348. Redistillation of fraction (4) afforded unchanged tri-*n*-butylamine. Fraction (6) had ultraviolet and infrared absorption properties indicating the major component to be the pyridine (XVII); additional infrared absorption bands in the region 3350—3200 $cm.^{-1}$ suggested the presence of some $-NH-$ groupings.

Reaction of cyclo*Pentanone with* N-cyclo*Pentylidene*-n-*butylamine at* 200° (Table 1, Expt. 7).—(a) *Basic products.* This material (76 g.) was heated at 100° for 2 hr. with acetic anhydride (76 ml.) containing concentrated sulphuric acid (0·5 ml.), and then separated into acetylated and non-acetylated components. Distillation of the tertiary bases (63·5 g.) afforded fractions:

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(1) (4·32 g.) b. p. 91—130°/0·2 mm.; (2) (8·30 g.) b. p. 130—146°/0·2 mm.; (3) (4·82 g.) b. p. 146—160°/0·2 mm.; a viscous residue (44·50 g.) remained. Fractions (1) and (2) were recombined and redistilled, to give fractions: (4) (1·23 g.) b. p. 80—99°/0·15 mm., n_D^{22} 1·4928; (5) (8·93 g.) b. p. 99—108°/0·15 mm., n_D^{22} 1·5390; (6) (1·47 g.) b. p. 138—148°/0·2 mm., n_D^{22} 1·5533. Of these, fraction (5) gave 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*pentenopyridine (8·08 g.), b. p. 90°/0·1 mm., n_D^{22} 1·5407 (Found: C, 83·2; H, 9·6; N, 7·0%) [light and infrared spectra; chloroplatinate m. p. and mixed m. p. 187° (decomp.)].

(b) *Non-basic products.* When distilled, this material (51·5 g.) yielded fractions: (7) (2·08 g.) b. p. 34—80°/22 mm., n_D^{22} 1·4215; (8) (11·44 g.) b. p. 80—140°/22 mm., n_D^{22} 1·4859: (9) (12·80 g.) b. p. 100—176°/0·18 mm., n_D^{22} 1·5255.

Fraction (7) was unchanged *cyclo*pentanone. Fraction (8) was a mixture of 2-*cyclo*pentyl-*cyclo*pentanone (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 157—158°) and 2-*cyclo*pentylidene*cyclo*pentanone [2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 228—229° decomp.)]. The mass spectrum of fraction (9) had peaks at mass : charge ratios 218 (weak), 216, 206, 152 (weak), 150, and 84, attributable to *x*-*cyclo*pentyl-2-*cyclo*pentylidene*cyclo*pentanone, 2-(2′-*cyclo*pentylidene*cyclo*pentylidene)*cyclo*pentanone, *x*-butyl-2-*cyclo*pentylidene-*cyclo*pentanone, 2-*cyclo*pentyl*cyclo*pentanone, 2-*cyclo*pentylidene*cyclo*pentanone, and *cyclo*pentanone respectively; additional peaks of unknown origin were found at mass : charge ratios 249, 251, 265, and 267. This fraction (2·20 g.) yielded x-*butyl*-2-cyclo*pentylidene*cyclo*pentanone* 2 : 4-*dinitrophenylhydrazone* (?) (1·0 g.), red needles (from ethyl acetate), m. p. 190° (Found: C, 61·3; H, 6·5; N, 14·6. $C_{20}H_{26}O_4N_4$ requires C, 62·2; H, 6·8; N, 14·5%). A satisfactory crystalline semicarbazone could not be isolated from this fraction.

Reaction of 2-cyclo*Pentylidene*cyclo*pentanone with* n-*Butylamine at* 200° (Table 1, Expt. 8).—(a) *Basic products.* This material (77 g.) was treated at 100° during 3 hr. with acetic anhydride (75 ml.) containing concentrated sulphuric acid (0·5 ml.), and then was separated into acetylated and non-acetylated bases. Distillation of the non-acetylated bases afforded fractions: (1) (3·54 g.) b. p. 118—124°/0·4 mm.; (2) (9·08 g.) b. p. 124—138°/0·4 mm.; (3) (3·49 g.) b. p. 140—150°/0·4 mm. Fractions (1) and (2) were recombined and gave 4-*n*-propyl-2 : 3-5 : 6-di*cyclo*-pentenopyridine (10·41 g.), b. p. 95°/0·1 mm., n_D^{22} 1·5405 (Found: C, 83·6; H, 9·0; N, 7·1%) [light and infrared spectra; chloroplatinate, m. p. and mixed m. p. 192° (decomp.)].

(b) *Non-basic products.* When distilled, this material (105·7 g.) yielded fractions: (4) (4·23 g.) b. p. 30—80°/20 mm., n_D^{22} 1·4290; (5) (25·20 g.) b. p. 90—130°/20 mm., n_D^{22} 1·4979; (6) (21·58 g.) b. p. 64—126°/0·1 mm., n_D^{22} 1·5272; (7) (2·09 g.) b. p. 126—140°/0·1 mm., n_D^{22} 1·5528; a viscous residue (49·6 g.) remained.

Fraction (4) was *cyclo*pentanone [semicarbazone, m. p. and mixed m. p. 217—218° (decomp.); 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 144°]. Fraction (5) was a mixture of 2-*cyclo*pentyl*cyclo*pentanone and 2-*cyclo*pentylidene*cyclo*pentanone. The mass spectrum of fraction (6) had parent peaks at mass : charge ratios 218, 216, 206, 152, 150, and 84, due respectively to *x*-*cyclo*pentyl-2-*cyclo*pentylidene*cyclo*pentanone, 2-(2′-*cyclo*pentylidene*cyclo*pentylidene)*cyclo*pentanone, *x*-butyl-2-*cyclo*pentylidene*cyclo*pentanone, 2-*cyclo*pentyl*cyclo*pentanone, 2-*cyclo*pentylidene*cyclo*pentanone, and *cyclo*pentanone; other, unidentified, peaks at mass : charge ratios 189, 171, 163, and 161, were found. This fraction yielded x-cyclo*pentyl*-2-cyclo*pentylidene*cyclo*pentanone* 2 : 4-*dinitrophenylhydrazone* (?), scarlet needles (from ethyl acetate), m. p. 210° (Found: C, 63·9; H, 6·3; N, 14·1. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·6; N, 14·1%). The crystalline fraction (7) was mainly the ketone (XI), m. p. and mixed m. p. 80°.

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798. *Studies of Trifluoroacetic Acid. Part XVI.* The Use of* 1 : 3-2 : 4-*Di*-O-*ethylidene*-6-O-*trifluoroacetyl*-D-*glucitol in the Synthesis of Some* 5- *and* 6-*Substituted* D-*Glucitols.*

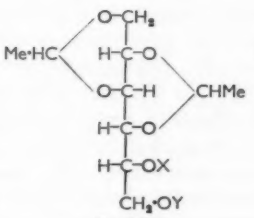
By E. J. Bourne, (Mrs.) C. E. M. Tatlow, J. C. Tatlow, and R. Worrall.

Trifluoroacetylation of 1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol gave the 5 : 6-bistrifluoroacetate, from which, by controlled alcoholysis, the 6-trifluoroacetate was obtained. The latter with acetic anhydride–pyridine or with acetic acid–trifluoroacetic anhydride gave the 5-acetate 6-trifluoroacetate, which was converted into the 5-acetate by alcoholysis. Toluene-*p*-sulphonylation of this afforded the known 5-acetate 6-toluene-*p*-sulphonate. Methylation of the 5-acetate, or of the 5-acetate 6-trifluoroacetate, gave, by a process involving acetyl migration, the 6-*O*-acetyl-5-*O*-methyl derivative. This was converted by deacetylation into 1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol, which was prepared also from the known 6-benzoate ester of this series by methylation and debenzoylation.

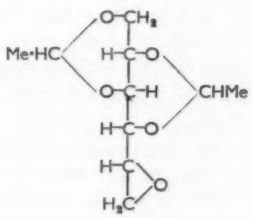
This paper describes another example of the use of the trifluoroacetyl residue as a blocking group in organic synthesis. Since our preparation of partially substituted glucoses from trifluoroacetate ester intermediates,[1] other investigations have been carried out on carbohydrates,[2] polypeptides,[3] and other compounds.[4,5] *O*-Trifluoroacetyl residues can be removed by alcoholysis, and *N*-trifluoroacetyl residues by hydrolysis with very mild alkali, so that whilst they can protect hydroxyl or amino-groups during many reactions at other centres in a molecule, they can subsequently be removed easily and selectively.

	X	Y
(I)	H	H
(II)	CF_3·CO	CF_3·CO
(III)	H	CF_3·CO
(IV)	Ac	CF_3·CO
(V)	Ac	H
(VI)	Ac	Ts

	X	Y
(VII)	Me	Ac
(VIII)	Me	H
(IX)	H	Bz
(X)	Me	Bz
(XI)	H	Me
(XIII)	Ac	Me
(XIV)	Bz	H



(I—XI)
(XIII, XIV)



(XII)

The present work, which was completed several years ago, started from 1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (I). This, with trifluoroacetic anhydride–sodium trifluoroacetate, gave the 5 : 6-bistrifluoroacetate (II). Controlled alcoholysis of this diester (II) with *iso*pentyl alcohol removed one trifluoroacetyl residue, to give a 1 : 3-2 : 4-di-*O*-ethylidene-*O*-trifluoroacetyl-D-glucitol (III). The monoester (III) was acetylated, with formation of the diester (IV), whence methyl alcohol removed the trifluoroacetyl group, giving an acetate (V), toluene-*p*-sulphonylation of which afforded the known 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-tosyl-D-glucitol [6] (VI).

* Part XV, *J.*, 1958, 3268.

[1] Bourne, Tatlow, and Tatlow, *J.*, 1950, 1367; Bourne, Stacey, Tatlow, and Tatlow, *J.*, 1951, 826.
[2] Bourne, Huggard, and Tatlow, *J.*, 1953, 735; Butler, Lloyd, and Stacey, *J.*, 1955, 1531.
[3] Taurog, Abraham, and Chaikoff, *J. Amer. Chem. Soc.*, 1953, **75**, 3473; Weygand and Leising, *Chem. Ber.*, 1954, **87**, 248; Weygand and Reiher, *Chem. Ber.*, 1955, **88**, 26; Schallenberg and Calvin, *J. Amer. Chem. Soc.*, 1955, **77**, 2779.
[4] Lardon and Reichstein, *Helv. Chim. Acta*, 1954, **37**, 388.
[5] Reed, *J. Amer. Chem. Soc.*, 1956, **78**, 801.
[6] Wiggins, *J.*, 1946, 388.

Treatment of the acetate (V) with methyl iodide and silver oxide gave an *O*-acetyl *O*-methyl ether (VII), m. p. 92°, which was obtained similarly from the acetate trifluoroacetate (IV). It has been found before [1] that trifluoroacetyl groups are replaced by methyl in reactions involving the Purdie reagents. The ether acetate (VII) was deacetylated to a 1 : 3-2 : 4-di-*O*-ethylidene-*O*-methyl-D-glucitol (VIII), m. p. 88—89°. The structures of these two methyl ethers (VII and VIII) were established by independent syntheses of both the 5- and the 6-*O*-methyl derivative of 1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol. The 5-*O*-methyl derivative was made from the known 6-*O*-benzoyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol [7,8] (IX) by methylation with methyl iodide–silver oxide, followed by debenzoylation. Benzoyl migration is very unlikely during this methylation since it is known [8] that in this series benzoyl groups migrate from $C_{(5)}$ to $C_{(6)}$. The 6-benzoate (IX) was unchanged after treatment with silver oxide in refluxing acetone. The 5-methyl ether produced in this way had m. p. 87—88°, undepressed in admixture with compound (VIII), and afforded a 6-acetate, m. p. 93°, undepressed in admixture with compound (VII). 1 : 3-2 : 4-Di-*O*-ethylidene-6-*O*-methyl-D-glucitol (XI) was prepared by the method of Vargha and Puskas,[9] by reaction of the corresponding 5 : 6-anhydro-derivative (XII) with sodium methoxide. The product, which is that expected from the general mode of scission of anhydro-rings,[10] had m. p. 70°, depressed on admixture with either compound (VIII) or the sample of the 5-*O*-methyl ether prepared from the 6-benzoate (IX). Acetylation of the 6-*O*-methyl derivative (XI) gave its 5-acetate (XIII), m. p. 95—96°, depressed on admixture with either sample of compound (VII) described above. Thus, the ether (VIII) must have been 1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol, and compound (VII) the corresponding 6-*O*-acetyl ester.

The acetylation of the monotrifluoroacetate (III) was next studied, with acetic acid–trifluoroacetic anhydride.[11] There was obtained an acetate trifluoroacetate whose crystalline form differed from that of compound (IV) and whose melting point was somewhat lower than that of (IV) (though with no depression on admixture). However, this new sample and compound (IV) gave the same acetate (V), acetate toluene-*p*-sulphonate (VI), acetate methyl ether (VII), and methyl ether (VIII). Further, the specimens of this acetate trifluoroacetate (IV) had identical infrared spectra (in Nujol; 1900—600 $cm.^{-1}$). Thus, the two different methods of acetylation gave the same product, contrary to the results obtained [1] with methyl 4 : 6-*O*-benzylidene-α-D-glucoside. Benzene was used as a solvent in the acetylation with acetic acid–trifluoroacetic anhydride, and from later results [11b] on this acylation process the presence of a non-polar solvent may have given rise to some bistrifluoroacetate as well as acetate trifluoroacetate. The slight difference in properties of the second sample of the latter may have been due to contamination by a trace of the bistrifluoroacetate, but, from the analytical results, the amount present, if any, must have been very small.

The above observations on the acetate (V) were at first sight contradictory, since it had given rise to a 5-*O*-acetyl-6-*O*-tosyl derivative (VI), and to a 6-*O*-acetyl-5-*O*-methyl ether (VII). However, examples of acyl migrations during methylations with the Purdie reagents are quite common,[12,13] whereas, in general, toluene-*p*-sulphonylation in pyridine appears not to cause such wanderings of groups. After treatment with pyridine, the acetate (V) was recovered in good yield, whereas silver oxide in refluxing acetone gave a syrup. Though no definite new compound could be isolated from this, no starting material was recovered and no crystalline toluenesulphonate was obtained. Further, in general,[13]

[7] Sullivan, *J. Amer. Chem. Soc.*, 1945, **67**, 837.
[8] Heyns and Stein, *Annalen*, 1947, **558**, 194.
[9] Vargha and Puskas, *Ber.*, 1943, **76**, 859.
[10] Wiggins and Wood, *J.*, 1950, 1566; Wiggins, *Adv. Carbohydrate Chem.*, 1950, **5**, 191.
[11] (*a*) Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976; Bourne, Stacey, Tatlow, and Worrall, *J.*, 1954, 2006; (*b*) *Idem*, *J.*, 1958, 3268.
[12] Haworth, Hirst, and Teece, *J.*, 1931, 2858.
[13] Sugihara, *Adv. Carbohydrate Chem.*, 1953, **8**, 1.

acetyl migration occurs towards a primary hydroxyl group; again, 5-*O*-benzoyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol [8] (XIV) when treated with alkali but migration in the reverse direction was not observed. Thus, all the evidence indicates that the monoacetate (V) is 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol, and that acetyl migration to $C_{(6)}$ occurred during the methylation with methyl iodide–silver oxide. Attempts to convert the 5-acetate (V) into the 6-acetate by mild alkali gave syrups from which neither starting material nor the 6-*O*-acetate could be isolated. The allocation of the 5-acetate structure to compound (V) means that its precursors (III) and (IV) are probably both 6-*O*-trifluoroacetyl esters. This would be expected, since the foregoing discussion suggests that in the bistrifluoroacetate (II), the 6-*O*-trifluoroacetyl group is the more stable and the trifluoroacetyl carried on the secondary 5-alcoholic group should be removed preferentially during alcoholysis.

Experimental

Unless otherwise stated, anhydrous conditions were used.

1 : 3-2 : 4-*Di*-O-*ethylidene*-D-*glucitol*.—Syrupy tri-*O*-ethylidene-D-glucitol [14] was hydrolysed by Appel's procedure [15] to **1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol** (15%), m. p. 210—212°, $[\alpha]_D^{17}$ −11·6° (*c* 4·33 in H_2O). Cited values [14] were m. p. 212—213°, $[\alpha]_D^{15}$ −10·9° (*c* 5·5 in H_2O).

1 : 3-2 : 4-*Di*-O-*ethylidene*-5 : 6-*bis*-O-*trifluoroacetyl*-D-*glucitol*.—1 : 3-2 : 4-Di-*O*-ethylidene-D-glucitol (4·00 g.) was treated with trifluoroacetic anhydride (18·2 g.) and sodium trifluoroacetate (1·00 g.) at 60° for 20 min.; complete solution was achieved. The mixture was then distilled under slightly diminished pressure with several portions of carbon tetrachloride and the residue was extracted with boiling carbon tetrachloride (3 × 25 c.c.). The combined extracts were filtered and evaporated. Recrystallisation of the residue from light petroleum (b. p. 60—80°) afforded **1 : 3-2 : 4-*di*-O-*ethylidene*-5 : 6-*bis*-O-*trifluoroacetyl*-D-*glucitol*** (6·31 g.), m. p. 104—105°, $[\alpha]_D^{18}$ +6·7° (*c* 2·39 in $CHCl_3$) (Found: C, 39·5; H, 3·9; F, 26·3; $CF_3{\cdot}CO$, 45·4. $C_{14}H_{16}O_8F_6$ requires C, 39·4; H, 3·8; F, 26·7; $CF_3{\cdot}CO$, 45·5%).

Partial Alcoholysis of **1 : 3-2 : 4-*Di*-O-*ethylidene*-5 : 6-*bis*-O-*trifluoroacetyl*-D-*glucitol***.—(*a*) A solution of the bistrifluoroacetate (5·00 g.) in *iso*pentyl alcohol (250 c.c.; dried over $MgSO_4$) was kept at 25° for 42 hr. Light petroleum (b. p. 100—120°) (200 c.c.) was then added and the solution was evaporated under reduced pressure. The last traces of alcohol were removed by co-distillation with light petroleum (b. p. 100—120°), leaving a solid residue which was dissolved in acetone (20 c.c.). The precipitate (0·20 g.) (mainly diethylideneglucitol) formed on addition of light petroleum (b. p. 40—60°) (200 c.c.) to the acetone solution was removed and the clear filtrate was evaporated. The residue was recrystallised twice from light petroleum (b. p. 60—80°), giving **1 : 3-2 : 4-*di*-O-*ethylidene*-6-O-*trifluoroacetyl*-D-*glucitol*** (2·01 g.), m. p. 110—112°, depressed on admixture with the diester, $[\alpha]_D^{18}$ +6·4° (*c* 2·49 in $CHCl_3$) (Found: C, 43·5; H, 5·1; F, 17·4; $CF_3{\cdot}CO$, 29·3. $C_{12}H_{17}O_7F_3$ requires C, 43·6; H, 5·2; F, 17·3; $CF_3{\cdot}CO$, 29·4%). With *n*-pentyl alcohol, lower yields (*ca.* 30%) of the same monoester were obtained.

(*b*) **1 : 3-2 : 4-Di-*O*-ethylidene-D-glucitol** (5·00 g.) was warmed with trifluoroacetic anhydride (15·2 g.) and sodium trifluoroacetate (0·85 g.) at 60° for 20 min. and the crude bistrifluoroacetate was isolated as described previously. Without being recrystallised, this was dissolved in *iso*pentyl alcohol (400 c.c.) and after 40 hr. at 25° the solution was worked up as above, to give **1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-trifluoroacetyl-D-glucitol** (3·43 g.), m. p. and mixed m. p. 110—112°, $[\alpha]_D^{18}$ +6·5° (*c* 2·48 in $CHCl_3$).

Acetylation of **1 : 3-2 : 4-*Di*-O-*ethylidene*-6-O-*trifluoroacetyl*-D-*glucitol***.—Acetic anhydride (1·08 g.) was added to a solution of the 6-trifluoroacetate (1·71 g.) in pyridine (3 c.c.). After 44 hr. at 25°, the mixture was distilled under diminished pressure with several portions of carbon tetrachloride. The residue, recrystallised twice from light petroleum (b. p. 60—80°), gave **5-O-*acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-6-O-*trifluoroacetyl*-D-*glucitol*** (1·35 g.), needles, m. p. 94—98°, $[\alpha]_D^{21}$ +5·7° (*c* 2·46 in $CHCl_3$) (Found: C, 44·9; H, 4·9; F, 15·5%; N-alkali uptake, 5·39 c.c./g. $C_{14}H_{19}O_8F_3$ requires C, 45·2; H, 5·1; F, 15·3%; N-alkali uptake, 5·37 c.c./g.).

5-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-D-*glucitol*.—The foregoing diester (0·504 g.) in methyl alcohol (10 c.c.) was kept at 20° for 30 min. before the alcohol was removed under reduced

[14] Bourne and Wiggins, *J.*, 1948, 1933.
[15] Appel, *J.*, 1935, 425.

pressure. Recrystallised from light petroleum (b. p. 80—100°), the product, 5-O-*acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-D-*glucitol* (0·187 g.), had m. p. 134—135°, $[\alpha]_D^{20}$ +1·1° (*c* 3·05 in $CHCl_3$) (Found: C, 52·5; H, 7·2; Ac, 15·7. $C_{12}H_{20}O_7$ requires C, 52·2; H, 7·3; Ac, 15·6%).

Difficulty was experienced at first in obtaining consistent yields of the monoester from this alcoholysis. One sample of methyl alcohol gave syrups, from another the starting material was recovered. Methyl alcohol, which had been dried with magnesium and iodine [16] and purified by distillation through a 1 foot column packed with glass helices, gave reproducible yields of 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol.

5-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-6-O-*tosyl*-D-*glucitol*.—Toluene-*p*-sulphonyl chloride (0·071 g.) was added to 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·082 g.) in pyridine (0·2 c.c.), and the solution kept at 25° for 20 hr. before being poured into water–chloroform. The chloroform layer was separated and the aqueous layer was extracted once more with chloroform. The combined extracts were dried ($MgSO_4$), filtered, and evaporated. The residue, recrystallised from light petroleum (b. p. 80—100°), gave 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-tosyl-D-glucitol (0·088 g.), m. p. 138° (alone and on admixture with an authentic specimen prepared by Wiggins's method [6]), $[\alpha]_D^{18}$ +5·0° (*c* 2·12 in $CHCl_3$). Wiggins [6] gave m. p. 140°, $[\alpha]_D^{17}$ +6·0° (*c* 1·664 in $CHCl_3$).

Treatment of 5-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-D-*glucitol with Pyridine*.—The specific rotation of a solution of 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·028 g.) in pyridine (1·00 c.c.) remained constant for 18 hr. at room temperature. The pyridine was removed by distillation under reduced pressure with several portions of light petroleum (b. p. 80—100°), and the residue, recrystallised from light petroleum (b. p. 80—100°), afforded the original 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·020 g.), m. p. and mixed m. p. 133—134°, $[\alpha]_D^{14}$ +0·9° (*c* 1·07 in $CHCl_3$).

6-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol*.—(*a*) Silver oxide (1·50 g.) was added to a solution of 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·565 g.) in methyl iodide (10 c.c.), and the mixture was refluxed for 15 hr. The methyl iodide was removed by distillation, and the residue extracted exhaustively with boiling chloroform. Distillation of the filtered extracts left a solid, which, when recrystallised from light petroleum (b. p. 60—80°), afforded 6-O-*acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol* (0·397 g.), m. p. 92° [not depressed on admixture with a specimen (m. p. 93°) synthesised by another route (see below) but depressed on admixture with 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-methyl-D-glucitol (m. p. 95—96°)], $[\alpha]_D^{17}$ −0·3° (*c* 3·98 in $CHCl_3$) (Found: C, 54·1; H, 8·0; Ac, 15·3; OMe, 10·7. $C_{13}H_{22}O_7$ requires C, 53·8; H, 7·6; Ac, 14·8; OMe, 10·7%).

(*b*) A solution of 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-trifluoroacetyl-D-glucitol (1·95 g.) in methyl iodide (10 c.c.) was refluxed for 18 hr. with silver oxide (4·00 g.). The product was isolated as above, and recrystallised from light petroleum (b. p. 60—80°), giving 6-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (0·781 g.), m. p. 91—92° (alone and in admixture with the specimen prepared as above), $[\alpha]_D^{21}$ ±0·0° (*c* 10·78 in $CHCl_3$).

1 : 3-2 : 4-*Di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol from* 6-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol*.—A small piece of sodium was added to 6-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (0·507 g.) in magnesium-dried methanol (10 c.c.) and the solution was kept at room temperature for 16 hr. Solid carbon dioxide was then added, the solution evaporated to dryness and the residue was extracted exhaustively with boiling chloroform. Distillation of the filtered extracts and recrystallisation from light petroleum (b. p. 60—80°) gave 1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol* (0·253 g.), m. p. 88—89° [not depressed on admixture with an authentic specimen (m. p. 87—88°) (see below), but depressed on admixture with 1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-methyl-D-glucitol (m. p. 70°)], $[\alpha]_D^{19}$ −5·0° (*c* 2·39 in $CHCl_3$) (Found: C, 53·1; H, 8·2; OMe, 12·2. $C_{11}H_{20}O_6$ requires C, 53·2; H, 8·1; OMe, 12·5%).

The same product (yield 27%) was isolated from the mother-liquors of the acetyl determination on the 5-methyl ether 6-acetate.

Treatment of 5-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-D-*glucitol in Acetone with Silver Oxide*.—Silver oxide (1·0 g.) was heated with 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·080 g.) in acetone (10 c.c.) for 18 hr. The acetone was distilled off and the residue extracted exhaustively with boiling chloroform. Distillation of the filtered extracts left a syrup (0·060 g.).

Acetylation of 1 : 3-2 : 4-*Di*-O-*ethylidene*-6-O-*trifluoroacetyl*-D-*glucitol*.—(a) *Isolation of the*

[16] Vogel, " A Text Book of Organic Chemistry," Longmans, Green and Co., London, 1948, p. 168.

product. A mixture of acetic acid (0·20 g.) and trifluoroacetic anhydride (0·75 g.) was added to 1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-trifluoroacetyl-D-glucitol (0·967 g.) in benzene (12 c.c.). After 20 min. at 60°, carbon tetrachloride (20 c.c.) was added and the solution was evaporated under reduced pressure. The residue was re-acetylated as before for 15 min., and the mixture was distilled under reduced pressure with carbon tetrachloride (4 × 25 c.c.). The solute, recrystallised twice from light petroleum (b. p. 40—60°), afforded 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-trifluoroacetyl-D-glucitol (0·696 g.), plates, m. p. 88—89°, $[\alpha]_D^{18}$ +7·7° (*c* 2·63 in $CHCl_3$) (Found: C, 45·0; H, 5·1; F, 15·3%; N-alkali uptake, 5·36 c.c./g.).

(b) *Properties.* This sample (plates, m. p. 88—89°) did not depress the m. p. of the material (needles, m. p. 94—98°) obtained by acetylation of 1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-trifluoroacetyl-D-glucitol with acetic anhydride and pyridine. The infrared spectra of the two samples in Nujol were identical over the frequency range 1900—600 $cm.^{-1}$. The difference in m. p. may be attributed to their different crystalline forms, or to a trace of impurity, *e.g.*, the bistrifluoroacetate. Methylation afforded the 6-*O*-acetate 5-*O*-methyl ether (51%), m. p. and mixed m. p. 92—93°, deacetylated by sodium methoxide in methanol to the 5-*O*-methyl ether (59%), m. p. and mixed m. p. 88—89°.

Methanolysis of this sample of the acetate trifluoroacetate gave the 5-acetate (51%), m. p. and mixed m. p. 134—135°, which by tosylation was converted into the 5-*O*-acetate 6-*O*-toluene-*p*-sulphonate (64%), m. p. and mixed m. p. 138°. These four derivatives had correct specific rotations.

1 : 3-2 : 4-*Di*-O-*ethylidene*-6-O-*methyl*-D-*glucitol.*—Prepared [9] by the action of excess of methanolic sodium methoxide on 5 : 6-anhydro-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol, 1 : 3-2 : 4-di-*O*-ethylidine-6-*O*-methyl-D-glucitol had m. p. 70°, $[\alpha]_D^{19}$ +4·6° (*c* 2·17 in $CHCl_3$). Cited values [9] were m. p. 70°, $[\alpha]_D^{20}$ +4·5° (*c* 2·65 in $CHCl_3$). The m. p. of this compound was depressed on admixture with all samples of 1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (m. p. 88—89°).

5-O-*Acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-6-O-*methyl*-D-*glucitol.*—Acetic anhydride (1·08 g.) was added to 1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-methyl-D-glucitol (0·319 g.) in pyridine (1·0 c.c.) and the solution was kept at 25° for 18 hr. before being poured into water and extracted with chloroform. The extracts were washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and with water, and after being dried ($MgSO_4$) were evaporated. The residue, recrystallised from light petroleum (b. p. 60—80°), afforded 5-O-*acetyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-6-O-*methyl*-D-*glucitol* (0·286 g.), m. p. 95—96°, $[\alpha]_D^{18}$ +0·9° (*c* 2·15 in $CHCl_3$) (Found: C, 54·0; H, 7·3. $C_{13}H_{22}O_7$ requires C, 53·8; H, 7·6%). This compound depressed the m. p. of all samples of 6-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (m. p. 92°).

6-O-*Benzoyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol.*—Silver oxide (8·0 g.) was refluxed with 6-*O*-benzoyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol [7] (2·92 g.) in methyl iodide (30 c.c.) for 18 hr. The methyl iodide was removed and the residue was exhaustively extracted with boiling chloroform. The filtered extracts were evaporated and the residual syrup was re-methylated with silver oxide (3·0 g.) and methyl iodide (15 c.c.), and then the product isolated as before. Recrystallisation of the residue from light petroleum (b. p. 60—80°) afforded 6-O-*benzoyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol* (1·84 g.), m. p. 95—96°, $[\alpha]_D^{23}$ −0·2° (*c* 8·56 in $CHCl_3$) (Found: C, 61·7; H, 7·0; OMe, 8·8. $C_{18}H_{24}O_7$ requires C, 61·4; H, 6·9; OMe, 8·8%).

A solution of 6-*O*-benzoyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·215 g.) in acetone (20 c.c.) was refluxed with silver oxide (1·0 g.) for 18 hr. before the solute was isolated as above. Recrystallisation from light petroleum (b. p. 80—100°) afforded the original 6-*O*-benzoyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol (0·155 g.), m. p. and mixed m. p. 164—166°, $[\alpha]_D^{19}$ +3·9° (*c* 1·54 in $CHCl_3$).

1 : 3-2 : 4-*Di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol and its* 6-*Acetate from* 6-O-*Benzoyl*-1 : 3-2 : 4-*di*-O-*ethylidene*-5-O-*methyl*-D-*glucitol.*—6-*O*-Benzoyl-1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (1·18 g.) was heated under reflux for 1 hr. with 0·4N-methanolic sodium hydroxide (25 c.c.). Solid carbon dioxide was then added and the solution was concentrated to *ca.* 3 c.c. and poured into water. The aqueous phase was extracted with chloroform and the combined extracts were washed with water, dried ($MgSO_4$), and evaporated. Recrystallised from light petroleum (b. p. 60—80°), the residue, 1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (0·600 g.), had m. p. 87—88°, $[\alpha]_D^{20}$ −4·8° (*c* 1·66 in $CHCl_3$). The m. p. of this compound was not depressed on admixture with the 1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (m. p.

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88—89°) obtained from 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-D-glucitol, but it was depressed on admixture with 1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-methyl-D-glucitol (m. p. 70°).

Acetic anhydride (0·50 g.) was added to a solution of 1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (0·198 g.) in pyridine (0·5 c.c.) and the solution was kept at 25° for 18 hr., before being poured into water and extracted with chloroform. After isolation as usual the residue, recrystallised from light petroleum (b. p. 60—80°), afforded 6-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-5-*O*-methyl-D-glucitol (0·164 g.), m. p. 93°, $[\alpha]_D^{19}$ ±0·0° (*c* 2·05 in $CHCl_3$). This compound did not depress the m. p. of the samples described earlier (m. p. 92°), but with 5-*O*-acetyl-1 : 3-2 : 4-di-*O*-ethylidene-6-*O*-methyl-D-glucitol (m. p. 95—96°) considerable depressions of m. p. were given.

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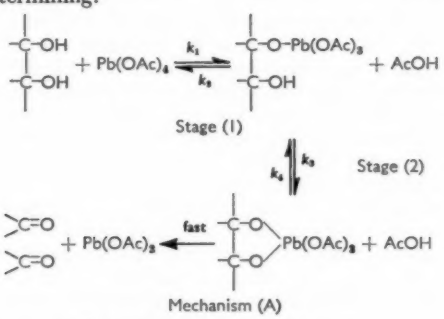
799. *Oxidations with Iodosobenzene Diacetate. Part VIII.* A Kinetic Study of the Oxidation of Benzpinacol.*

By L. K. DYALL and K. H. PAUSACKER.

Benzpinacol has been oxidised with iodosobenzene diacetate in both acetic acid–benzene and acetic acid–nitrobenzene between 16·30° and 66·65°. The enthalpies and entropies of activation, which varied appreciably as the composition of each mixed solvent was altered, were found to be linearly related, and the same solvent isokinetic relationship was obeyed in both solvent systems. The existence of isokinetic relationships in other glycol oxidations is discussed.

FROM a kinetic study of the oxidation of 1 : 2-diols with lead tetra-acetate in several solvents, Criegee, Kraft, and Rank [1] deduced mechanism (A) for the reaction. Since *cis*-diols would form a cyclic intermediate more readily than *trans*-diols, the fact that *cis*-diols are usually oxidised more rapidly than *trans*-diols can be explained if stage (2) is assumed to be rate-determining.



The equilibrium constant, K, for stage (1) is given by

$$K = [\text{AcOH}][\text{monoester}]/[\text{glycol}][\text{Pb(OAc)}_4]$$

whence $$[\text{monoester}] = K\,[\text{glycol}][\text{Pb(OAc)}_4]/[\text{AcOH}]$$

If $k_1 \sim k_2 \gg k_3 \gg k_4$, it follows that the rate of oxidation, k, is given by

$$k = \text{const.} \times K[\text{glycol}][\text{Pb(OAc)}_4]/[\text{AcOH}] \quad . \quad . \quad . \quad . \quad . \quad (1)$$

* Part VII, *Austral. J. Chem.*, 1957, **10**, 460.

[1] Criegee, Kraft, and Rank, *Annalen*, 1933, **507**, 159.

Relation (1) predicts that, if the concentration of acetic acid is reduced, the rate of oxidation will be increased, and partial confirmation was obtained by Criegee *et al.*[1] When a substantial proportion of an acetic acid solvent was replaced by benzene, nitrobenzene, dichloroethane, or tetrachloroethane, the rate of oxidation of *cyclo*hexane-1 : 2-diol was markedly increased. Later, Büchner and Criegee [2] found that addition of small amounts of water or methanol to an acetic acid solvent increased the rate of oxidation far more than could be accounted for by relation (1). It was suggested that, in these instances, lead tetra-acetate was solvolysed to a more active oxidant [Mechanism (B)]. Hydroxylic solvents able to react with the oxidant in this way were termed " active," while solvents unable so to react were termed " inert."

$$Pb(OAc)_4 + 2ROH \rightleftharpoons Pb(OAc)_2(OR)_2 + 2AcOH$$

Mechanism (B)

If a 1 : 2-diol is oxidised in an inert solvent containing an excess of acetic acid, relation (1) predicts that the rate of oxidation is inversely proportional to the concentration of acetic acid. The present work was carried out to test the quantitative validity of this relation. Benzpinacol was oxidised in acetic acid–benzene and acetic acid–nitrobenzene solvents of varied composition. Benzene (dielectric constant $\varepsilon = 2{\cdot}38$) and nitrobenzene ($\varepsilon = 37{\cdot}8$) were chosen as the inert solvents to ensure that the changes in rate due to changes in the concentration of acetic acid ($\varepsilon = 9{\cdot}7$) could be differentiated from changes in rate due to variation of the dielectric constant of the solvent. It was found convenient to study the rates of oxidation with iodosobenzene diacetate; lead tetra-acetate and iodosobenzene diacetate are very similar in their action on 1 : 2-diols.[3,4,5]

Experimental

Purification of Materials.—Acetic acid was successively treated with chromic oxide and boron triacetate.[6] The anhydrous acid (m. p. 16·60°) thus prepared was too hygroscopic for convenient use, and was therefore diluted with distilled water to a water content of 0·15% by weight (m. p. 16·40°). Acrylonitrile was redistilled, b. p. 78°, immediately before use. Benzene was purified by Vogel's method [7] and dried over sodium wire.

Benzpinacol, prepared from benzophenone and propan-2-ol,[8] was crystallised three times from benzene–ligroin and had m. p. 188—189°. Iodosobenzene diacetate, prepared by Pausacker's method [3] and crystallised from benzene, had a minimum purity of 99·5%. The purity was checked at weekly intervals. Nitrobenzene, thoroughly washed with 2N-sodium hydroxide and distilled water in succession, was dried ($CaCl_2$) and distilled; b. p. 51°/0·1 mm., n_D^{15} 1·346.

Table 1. *Yield of benzophenone from the oxidation of benzpinacol with iodosobenzene diacetate in various solvents.*

	Inert solvent (ml.)	Acetic acid (ml.)	Benzophenone (yield %)
Benzene	50	0	96
	40	10	100
	25	25	84
	0	50	86
Nitrobenzene	45	5	91

Analysis of Products.—Benzpinacol (0·500 g.; 0·00137 mole) was oxidised, at room temperature, with iodosobenzene diacetate (0·490 g.; 0·00152 mole) in 50 ml. of the solvent of required composition. The course of the oxidation was followed by periodically removing a 1 ml. portion, adding it to acidified potassium iodide, and titrating the liberated iodine with

[1] Büchner and Criegee, *Ber.*, 1940, **73**, 563.
[2] Pausacker, *J.*, 1953, 107.
[3] Beucker and Criegee, *Ber.*, 1939, **541**, 218.
[4] Criegee, Höger, Huber, Kruck, Marktscheffel, and Schellenberger, *Annalen*, 1956, **599**, 81.
[5] Eichelberger and LaMer, *J. Amer. Chem. Soc.*, 1933, **55**, 3633.
[6] Vogel, " A Text Book of Practical Organic Chemistry," Longmans, London, 1950, p. 171.
[7] " Organic Syntheses," Wiley, New York, 1946, Coll. Vol. II, p. 71.

standardised sodium thiosulphate. When oxidation was complete, acetic acid and benzene were distilled off, and the oily residue of benzophenone and iodobenzene was crystallised from aqueous methanol or propan-2-ol. The benzophenone obtained was identified by determination of the m. p. and mixed m. p. When nitrobenzene was present the reaction mixture was treated with the theoretical quantity of 2 : 4-dinitrophenylhydrazine. Part of the expected yield of benzophenone 2 : 4-dinitrophenylhydrazone (m. p. and mixed m. p., 240—241°) crystallised, and the remainder was recovered by distilling off the solvent at reduced pressure and crystallising the residue from ethanol. The results of these analyses are given in Table 1.

Kinetic Procedure.—The temperature of the thermostat was controlled within ±0·03° if below 40°, or within ±0·12° if 40° or higher. The analytical procedure used was essentially that of Cordner and Pausacker.[19] The first aliquot portion was removed 5—10 min. after mixing the preheated reactants, and the remaining eight portions were removed at intervals such that the reaction was followed from 15 to 60% completion. The time of half-outflow of the first portion into acidified potassium iodide was taken as zero time.

TABLE 2.

% AcOH (by vol.)	10^3k (mole^{-1} l. sec.$^{-1}$) 16·30°	25·65°	35·10°	40·04°	45·17°	E (kcal. mole^{-1})	$\log_{10} A$	$\Delta F^\ddagger$ (kcal. mole^{-1})	$\Delta H^\ddagger$	$-\Delta S^\ddagger$ (cal. deg.$^{-1}$)
(a) *Oxidation in acetic acid–benzene solvents*										
4	3·16	5·00	10·3	12·8	16·9	10·96	5·76	20·56	10·37	34·17
	3·34	5·37	11·5	13·7	16·8					
6	2·90	5·24	10·8	13·7	16·6	11·69	6·27	20·58	11·10	31·80
	2·85	5·31	10·0	13·7	17·3					
8	2·47	4·58	9·84	13·9	17·6	12·93	7·14	20·65	12·34	27·87
	2·47	4·90	10·2	14·6	17·6					
10	2·08	4·02	9·31	13·6	17·4	13·41	7·44	20·72	12·82	26·50
	1·98	4·07	9·69	13·1	17·6					
16	1·21	2·82	7·16	10·9	15·9	17·16	10·00	20·99	16·57	14·82
	1·11	2·81	7·03	10·7	14·9					
20	0·753	2·35	5·51	9·38	13·7	18·30	10·71	21·15	17·71	11·54
	0·806	2·16	5·65	8·89	13·4					
30	—	1·22	3·43	5·53	9·31	20·71	12·19	21·53	20·12	4·729
		1·25	3·48	5·72	9·37					
40	—	0·777	2·13	3·53	6·11	23·69	14·09	21·93	23·10	−3·924
		0·722	2·10	3·53	6·10					
60	—	—	—	1·73	3·13 *	21·36	12·17	22·11	20·77	4·494
				1·82	3·08 *					
100	—	—	—	1·82	2·67 †	21·15	11·99	22·24	20·56	5·601
				1·81	2·74 †					
(b) *Oxidation in acetic acid–nitrobenzene solvents*										
4	—	1·40	2·84	3·71	6·32	14·17	7·50	21·40	13·58	26·23
		1·31	2·81	3·92	5·72					
10	—	1·73	3·72	5·11	7·08	13·80	7·35	21·23	13·21	26·90
		1·77	3·66	5·61	7·21					
16	—	2·14	4·59	6·94	9·15	13·68	7·36	21·09	13·09	26·83
		2·32	4·66	6·54	8·85					
			4·81							
20	—	2·36	5·45	8·25	10·7	14·27	7·84	21·03	13·68	24·65
		2·40	5·47	7·81	9·81					
				8·05						
30	—	3·05	6·79	12·0	17·6	17·48	10·26	20·94	16·89	13·58
		2·97	7·61	13·7	16·9					
40	—	3·08	8·39	11·5	22·0	18·35	10·93	20·89	17·76	10·50
		3·30	8·67	11·9	23·6					
60	—	3·62	8·02	12·7	20·1	18·74	11·19	20·92	18·15	9·29
		3·76	8·19	13·2	19·9					
80	—	1·71	4·38	8·01	13·3	19·77	11·69	21·27	19·18	7·01
		1·76	4·54	7·71	13·3					

* At 56·15°, 10·7, 10·4; at 66·65°, 26·4, 25·6. † At 56·15°, 9·82, 10·5; at 66·65°, 24·3, 23·5.

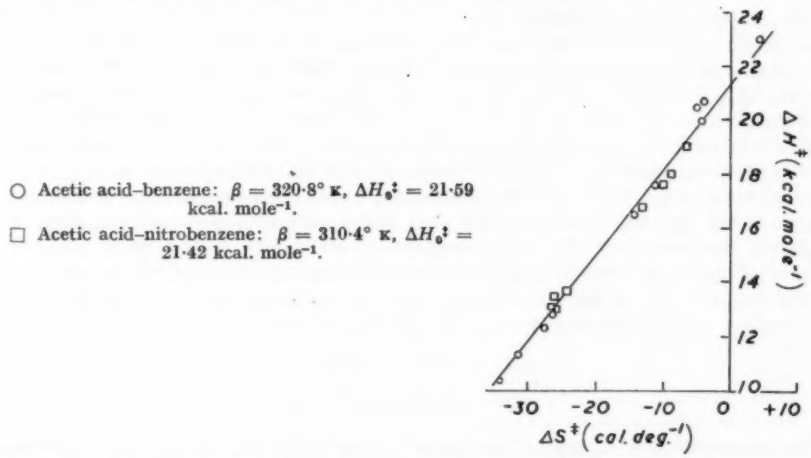
A solution of the oxidant in the solvent of composition used in the kinetic run was titrated before and after each run to check the stability of the oxidant; the deviation between the two titres never exceeded 0·5%.

Calculations.—A second-order rate constant was calculated for each aliquot portion titrated, and the arithmetic mean of the set of values was obtained. Variations from the mean were of a random nature, and did not exceed 5%.

The energy of activation, E, and the frequency factor, A, were calculated from the Arrhenius relationship by the method of least squares, and the enthalpy, $\Delta H^{\ddagger}$, free-energy change, $\Delta F^{\ddagger}$, and entropy, $\Delta S^{\ddagger}$, of activation at 25° were calculated by standard methods. By using these values of A and E, rate constants for each run were calculated from the Arrhenius equation; the mean deviation from the experimental values was 4·9% for acetic acid–benzene and 3·4% in acetic acid–nitrobenzene solvents. The results for both types of solvent are presented in Table 2.

Pure-order kinetics were not obtained when pure benzene or nitrobenzene was used as solvent; this is in agreement with observations by Criegee, Kraft, and Rank.[1]

Polymerisation Tests with Acrylonitrile.—The following mixtures were prepared: (i) A solution of benzpinacol (0·40 g.) and iodosobenzene diacetate (0·30 g.) in acetic acid (5 ml.), acrylonitrile (15 ml.), and benzene (30 ml.). (ii) A mixture of acetic acid (5 ml.), acrylonitrile (15 ml.), and benzene (30 ml.). (iii) A solution of benzpinacol (0·40 g.) in acetic acid (5 ml.), acrylonitrile (15 ml.), and benzene (30 ml.). (iv) A solution of iodosobenzene diacetate (0·30 g.) in acetic acid (5 ml.), acrylonitrile (15 ml.), and benzene (30 ml.).



The four solutions were kept in a thermostat at 45° for 1·5 hr. and then cooled to room temperature. Dry, peroxide-free ether was added to precipitate any polymerised acrylonitrile. White precipitates of the polymer settled from solutions (i) and (iv) only on standing overnight. Dilution with ether did not precipitate a polymer from either of these two solutions if the monomeric acrylonitrile was extracted with distilled water immediately after the period at 45°. Polymerisation therefore occurs only on prolonged contact with the oxidant, and not during the oxidation of the glycol.

Discussion

The relation (1) can now be tested. At a constant temperature, and at constant concentrations of benzpinacol and iodosobenzene diacetate, relation (2) should be obeyed.

$$k_V = k_{100} \times 100/V \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

k_V and k_{100} are the rates of reaction in solutions containing V% (v/v) and 100% acetic acid, respectively. Calculated values of k_V at 16·30° for acetic acid–benzene, and at 25·63° for acetic acid–nitrobenzene solvents, are shown in Table 3.

In acetic acid–benzene solvents, although the rate of reaction increases steadily as acetic acid is replaced by benzene, this increase is less than the calculated increase at concentrations greater than 40% (vol.) acetic acid, while at lower acetic acid concentrations

the rates are higher than expected. In acetic acid–nitrobenzene solvents the observed rate initially increases much more rapidly than that calculated but, as the acetic acid concentration decreases further, the observed rates actually diminish. Agreement between $k_{obs.}$ and k_T is no better at other temperatures. The effect of acetic acid concentration is therefore not as simple as predicted by relation (2). Evidently acetic acid exerts

TABLE 3. *Experimental and calculated rate constants in mixed solvents.*

Acetic acid–benzene (16·30°)						Acetic acid–nitrobenzene (25·63°)					
AcOH (vol. %)	$10^4k_{obs.}$	10^4k_T	AcOH (vol. %)	$10^4k_{obs.}$	10^4k_T	AcOH (vol. %)	$10^4k_{obs.}$	10^4k_T	AcOH (vol. %)	$10^4k_{obs.}$	10^4k
4	30·6	26·5	20	7·82	5·29	4	13·6	84·0	40	31·9	8·40
6	28·2	17·7	30	3·60	3·52	10	17·5	33·5	60	36·9	5·60
8	24·0	13·2	40	1·59	2·66	16	22·3	21·0	80	17·4	4·20
10	20·9	10·6	60	1·10	1·76	20	23·8	16·8	100	3·35	(3·35)
16	10·7	6·63	100	1·06	(1·06)	30	30·1	11·2			

appreciable solvation effects in addition to the predicted mass-action effect. Since the mechanism of the oxidation is not known with certainty, and kinetic measurements were made in the vicinity of the isokinetic temperature (see later), it is not possible to correlate solvent composition and oxidation rate.

In acetic acid–benzene solvents, $\log_{10} A$ varies from 5·76 to 14·09 (see Table 2), accompanied by corresponding changes in E (10·96—23·70 kcal. mole^{-1}). The relationship between $\log_{10} A$ and E is in fact linear, and a similar relationship exists in acetic acid–nitrobenzene solvents (Table 2) where $\log_{10} A$ varies from 7·35 to 11·99, and E from 13·68 to 21·15 kcal. mole^{-1}. These linear relationships indicate that a solvent isokinetic relationship [9] exists in each instance. In each solvent system, the enthalpy and entropy also vary over a wide range of values, and the relationship between these quantities is linear. The linearity of the plot has been tested for each mixed solvent system by evaluation of the correlation coefficient, r. The approximation of r to unity ($r = 0{\cdot}996$ in acetic acid–benzene solvents and 0·946 in acetic acid–nitrobenzene solvents) establishes the linearity beyond doubt.[9] The linear relationship may be expressed by equation (3) in acetic acid–benzene, and by equation (4) in acetic acid–nitrobenzene solvents.

$$\Delta H^{\ddagger} = 21{\cdot}59 + 320{\cdot}8\ \Delta S^{\ddagger} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$\Delta H^{\ddagger} = 21{\cdot}42 + 310{\cdot}4\ \Delta S^{\ddagger} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The linear enthalpy–entropy (" isokinetic ") relationship has recently been discussed by Leffler,[9] who showed that the two variables are correlated by equation (5).

$$\Delta H^{\ddagger} = \Delta H_0^{\ddagger} + \beta\,.\,\Delta S^{\ddagger} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

β is known as the isokinetic temperature, and at this temperature all reactions obeying the same isokinetic relationship will proceed at the same rate. β and the intercept $\Delta H_0^{\ddagger}$ have been calculated by the method of least squares for both solvent systems. The differences between the two isokinetic temperatures (48° in acetic acid–benzene solvents, 37° in acetic acid–nitrobenzene solvents) and the $\Delta H_0^{\ddagger}$ values (21·59 and 21·42 kcal. mole^{-1}, respectively) do not exceed the experimental errors, and it can be concluded that the same isokinetic relationship is obeyed in both solvent systems. The isokinetic temperature is actually within the temperature range at which the rate constants were measured, and the variations in rate as the solvent composition varied cannot therefore be regarded as significant.[9]

The kinetic data from several other investigations of the oxidation of glycols appear to obey isokinetic relationships. It is predicted by Büchner and Criegee's mechanism (B) that progressive addition of water to an acetic acid solvent should be accompanied by increases in the rate of oxidation of a 1 : 2-diol with lead tetra-acetate. Cordner and

[9] Leffler, *J. Org. Chem.*, 1955, **20**, 1202.

Pausacker,[10] however, found that the rate of oxidation of ethylene glycol increased to a maximum and then decreased as more water was added. The $\log_{10} A$ (10·96—14·51) and E (17·8—23·4 kcal. mole^{-1}) values are approximately linearly related, and, since the isokinetic temperature (60°) is in the vicinity of the temperatures (18—35°) at which kinetic measurements were made, a simple relationship between oxidation rate and solvent composition should not be expected. It is not certain that this is a solvent isokinetic relationship, since progressive addition of water to the acetic acid solvent may cause corresponding changes in the structure of the oxidant [Mechanism (B)].

The oxidation of pinacols with lead tetra-acetate in acetic acid solution [10] also appears to obey a structural isokinetic relationship ($\log_{10} A$, 10·52—14·87; E, 13·4—23·2 kcal. mole^{-1}). As the isokinetic temperature (95°) is well removed from the temperatures (18—35°) at which kinetic measurements were made, discussion of these results is probably valid.

An outstanding example of a structural isokinetic relationship is provided by the kinetic data obtained by Moriconi, O'Connor, and Wallenberger [11] for the oxidation of *cis*- and *trans*-9 : 10-diaryl-9 : 10-dihydrophenanthrene-9 : 10-diols. The $\log_{10} A$ values vary from 7·75 to 16·18, and E varies from 7·7 to 20·5 kcal. mole^{-1}. If the recalculated value of $A = 1{\cdot}42 \times 10^{15}$ for one *cis*-diol is used instead of the incorrect value of $1{\cdot}26 \times 10^{10}$ quoted by Moriconi *et al.*, the plot of $\log_{10} A$ versus E is linear. The isokinetic temperature (−25°) is 45—55° away from the temperatures used for the calculation of A and E values, and the detailed correlation between oxidation rate and diol structure made by these authors is therefore probably valid.

Isokinetic relationships may therefore be responsible for some of the difficulties [5] in correlating glycol structure or solvent composition with oxidation rate. Discussions based on rate constants determined at only one temperature, in the vicinity of the isokinetic temperature, are pointless if isokinetic relationships are obeyed by the reactions in question.

The mechanism of glycol oxidations has recently received considerable attention. The mechanism we previously suggested [10] involved initial condensation between the glycol and the oxidant to form a glycol monoester, followed by homolytic fission of the ester and abstraction of the remaining hydroxyl-group hydrogen atom of the glycol. Hey, Stirling, and Williams [12] have criticised this mechanism on the grounds that quantitative oxidation of glycols with iodosobenzene dibenzoate and lead tetrabenzoate occurs at temperatures much lower than those at which these oxidants are able to phenylate aromatic compounds. Moreover, the homolytic fission of the glycol ester would produce a radical more likely to attack the carbon-bound hydrogen atoms of the glycol than the hydrogen atom of a hydroxyl group. The first criticism may not be valid, since homolytic decomposition of the ester of the glycol with the oxidant is not strictly analogous to similar decomposition of the oxidant. The second objection is, however, a strong one, and appears to be supported by our failure to detect free radicals with acrylonitrile monomer during the oxidation of benzpinacol with iodosobenzene diacetate. It is also known now that hydrogen bonding of the glycol hydroxyl groups does not play a significant rôle.[5,11,13,14] We now suggest that the separation of the lead triacetoxy-group [see Mechanism (C)] is concomitant with attack on the adjacent hydroxyl group of the glycol. This mechanism is essentially an electron redistribution within a cyclic complex, and the distinction between homolytic and heterolytic fission is too fine to be drawn.[15,16]

Since a cyclic transition state involving both glycol hydroxyl groups is involved, this mechanism accounts for the observation that the ratio, k_{cis}/k_{trans}, of rates of oxidation of

[10] Cordner and Pausacker, *J.*, 1953, 102.
[11] Moriconi, O'Connor, and Wallenberger, *J. Amer. Chem. Soc.*, 1958, **80**, 656.
[12] Hey, Stirling, and Williams, *J.*, 1954, 2747.
[13] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[14] Kuhn, Moriconi, O'Connor, and Wallenberger, *J. Org. Chem.*, 1957, **22**, 1651.
[15] Hughes and Ingold, *Quart. Reviews*, 1952, **6**, 34.
[16] Buist and Bunton, *J.*, 1954, 1406.

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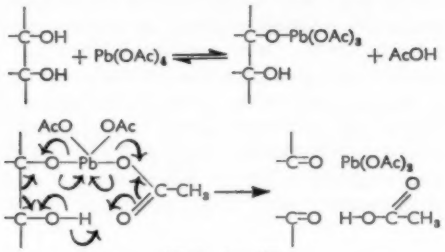
isomeric *cis*- and *trans*-glycols is usually greater than unity. It is not suggested, however, that this mechanism accounts for the oxidation of all glycols, and recent work by Levesley, Waters, and Wright [17] indicates that the ratio k_{cis}/k_{trans} is not always significant.



Mechanism (C)

The Brönsted-base mechanism (Criegee *et al.*,[5] Moriconi *et al.*,[11] Bell, Rivlin, and Waters [18]) is an alternative reaction path.

One of us (L. K. D.) is indebted to the Dunlop Rubber Company of Australia for a research scholarship.

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[*Received, May 15th*, 1958.]

[17] Levesley, Waters, and Wright, *J.*, 1956, 840.
[18] Bell, Rivlin, and Waters, *J.*, 1958, 1696.

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800. *Reduced Cyclic Compounds. Part VI.* The Preparation and Cyclisation of* trans-8-*Phenyloct-5-enoic and* trans-7-1′-*Naphthylhept-4-enoic Acid.*†

By M. F. ANSELL and S. S. BROWN.

The preparation, *via* the ring scission of 3-chlorotetrahydro-2-phenethyl- and -2-(2-1′-naphthylethyl)-pyran, of *trans*-8-phenyloct-5-enoic acid and *trans*-7-1′-naphthylhept-4-enoic acid is described. These acids with hot polyphosphoric acid yield respectively 1 : 2 : 3 : 7 : 8 : 9 : 10 : 10*a*-octahydro-7-oxo-*cyclo*hepta[*de*]naphthalene and 1 : 2 : 3 : 3*a* : 4 : 5-hexahydrobenz[*de*]anthr-6-one. On treatment with aluminium chloride in carbon disulphide, the phenyloctenoyl chloride yields 1 : 2 : 3 : 4 : 4*a* : 9 : 10 : 10*a*-octahydro-1-oxophenanthrene; the naphthylheptenoyl chloride resinifies.

SINCE reduced cyclic systems are formed by ring closure of ω-phenylalkenols [1] and by the intramolecular acylation [2] of alkenoic acids or acid chlorides, *trans*-8-phenyloct-5-enoic and *trans*-7-1′-naphthyl-hept-4-enoic acid (VII) were prepared and studied. The syntheses followed routes similar to those used [3] for alk-4- and -5-enoic acids. *trans*-7-Phenylhept-4-en-1-ol [1] gave *trans*-7-chloro-1-phenylhept-3-ene and thence, by carboxylation of the Grignard reagent, *trans*-8-phenyloct-5-enoic acid. Similar reactions from 3-chlorotetrahydro-2-(2-1′-naphthylethyl)furan yielded a difficultly separable mixture (cf. ref. 3) of *cis*- and *trans*-7-1′-naphthylhept-4-enoic acid. The pure *trans*-acid was however obtained by

* Part V, *J.*, 1958, 3388. † Cf. *Chem. and Ind.*, 1956, 980.

[1] Ansell and Selleck, *J.*, 1956, 1238.
[2] Ansell and Brown, *J.*, 1958, 2955.
[3] *Idem*, *J.*, 1957, 1788.

oxidation, with chromium trioxide–pyridine,[4] of *trans*-7-1′-naphthylhept-4-en-1-ol prepared by the ring scission of 3-chlorotetrahydro-2-(2-1′-naphthylethyl)pyran.

The ring closure of an arylalkenoic acid such as (I) to a tricyclic structure necessitates two intramolecular reactions—acylation and alkylation—and according to the order in which these occur, two different ring systems may be formed. Both cyclisation routes have been realised with *trans*-8-phenyloct-5-enoic acid. Treatment with hot polyphosphoric acid gave the tricyclic ketone (V) in good yield, evidently by way of the acid (IV) which is known [5] to afford the ketone (V) on treatment with hot polyphosphoric acid.

However, *trans*-8-phenyloct-5-enoyl chloride with aluminium chloride in boiling carbon disulphide (cf. ref. 6) gave mainly one ketone which on treatment with methylmagnesium iodide and then palladised charcoal afforded 1-methylphenanthrene (VI): the product was therefore the octahydro-1-oxophenanthrene (III), and in conformity had two closely spaced ultraviolet absorption maxima at *ca.* 270 mμ typical [1,7] of *as*-octahydrophenanthrene derivatives, and infrared absorption maxima at 13·3 and 5·9 μ as in the spectra of *o*-disubstituted benzenes and six-membered *cyclo*alkanones respectively.[8] The mechanism of cyclisation of the chloride of (I) ⟶ (III) and the stereochemistry of the product have not been elucidated. If acylation of the double bond and alkylation of the aromatic ring form a concerted process a *trans*-octahydrophenanthrene would result: [9] if acylation precedes alkylation, then 2-phenethyl*cyclo*hex-2-enone (II) is the effective intermediate. Although the ring closure of this ketone has been reported [10] to fail, there is no doubt that the reaction is practicable in view of the successful cyclisation [6] of 1-acetyl-2′-phenyl*cyclo*hexene. If, therefore, cyclisation of the acid chloride proceeds *via* a carbonium ion derived from (II), a mixture of *cis*- and *trans*-hydrophenanthrenes would be expected (cf. refs. 9 and 11); but since a virtually homogeneous product was obtained, equilibration to the more stable epimer seems likely to have occurred. For *as*-octahydrophenanthrene the *trans*-isomer is known [12] to be the more stable.

The ring closure of *trans*-7-1′-naphthylhept-4-enoic acid (VII) with polyphosphoric acid proved analogous to that of the acid (I); a good yield of 1 : 2 : 3 : 3*a* : 4 : 5-hexahydrobenz[*de*]anthr-6-one (IX) was obtained. This ketone, whose melting point was at variance with the only recorded value,[13] was identified by comparison with a specimen prepared by the action of polyphosphoric acid on β-(1 : 2 : 3 : 4-tetrahydro-1-phenanthryl)-propionic acid (VIII) itself obtained by reduction of β-(3 : 4-dihydro-1-phenanthryl)-propionic acid.[14] It is of interest that the cyclisation of the acid (VII) occurs in only one sense. Successive intramolecular alkylation and acylation of positions 8 and 9, respectively, would have yielded the 3 : 4-benzo-derivative of (V).

Attempted cyclisation of *trans*-7-1′-naphthylhept-4-enoyl chloride with aluminium chloride in carbon disulphide at temperatures from −10° to +46° gave tars, from which only traces of ketonic material were isolated. If, as expected (cf. ref. 2), 2-(2-1′-naphthylethyl)*cyclo*pent-2-enone (X) were the initial product, this should cyclise further [probably to (XI) [15]] or be recovered unchanged (cf. refs. 10 and 16). It must be assumed that intermolecular acylation of the reactive nucleus is faster than intramolecular acylation of the double bond, and so gives rise to polymers.

[4] Poos, Arth, Beyler, and Sarrett, *J. Amer. Chem. Soc.*, 1953, **75**, 422; Poos, Johns, and Sarrett, *ibid.*, 1955, **77**, 1026.
[5] Gilmore and Horton, *ibid.*, 1951, **73**, 1411.
[6] Gutsche and Johnson, *ibid.*, 1946, **68**, 2239.
[7] Askew, *J.*, 1935, 512.
[8] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, Chapters 5 & 9.
[9] Stork and Burgstahler, *J. Amer. Chem. Soc.*, 1955, **77**, 5068.
[10] Cohen and Cook, *J.*, 1935, 1570.
[11] Barnes and Olin, *J. Amer. Chem. Soc.*, 1956, **78**, 3830.
[12] Cook, McGinnis, and Mitchell, *J.*, 1944, 286.
[13] Hoch, *Compt. rend.*, 1938, **207**, 921.
[14] Johnson, Peterson, and Schneider, *J. Amer. Chem. Soc.*, 1947, **69**, 74.
[15] Johnson and Posvic, *ibid.*, p. 1361.
[16] Harper, *J.*, 1937, 1859.

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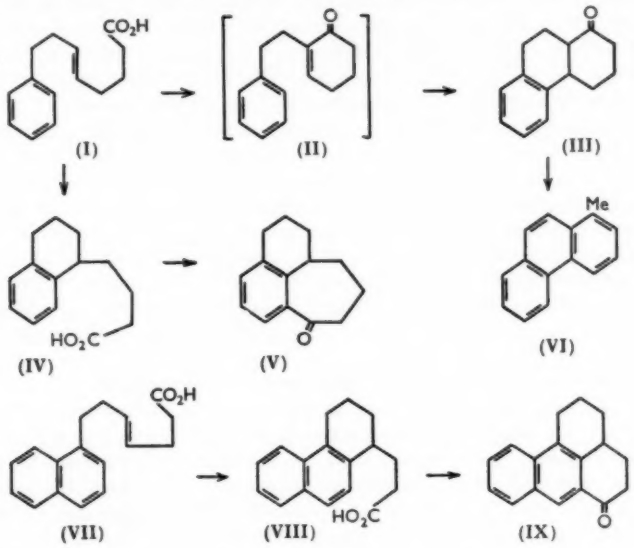
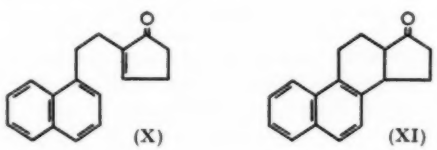
Acid-catalysed " double ring-closures," such as those described above, constitute a novel route to hydroaromatic ketones of the types (III), (V), and (IX). Cyclisation of these ω-arylalkenoic acids may be regarded as a logical extension of those reactions in



which an olefinic acid undergoes intermolecular condensation with an aromatic hydrocarbon to form a polycyclic system, as exemplified by the preparation of 1-methyl-3′-oxo-2 : 3-*cyclo*pentanoacenaphthene from acenaphthene and crotonic acid,[17] of 1-tetralone from benzene and γ-butyrolactone,[18] and of 3 : 4-benzopyrene-1 : 5-quinone from phthalidyleneacetic acid and naphthalene.[19]



Experimental

Ultraviolet absorption spectra were measured for 95% ethanol solutions.

trans-7-*Chloro*-1-*phenylhept*-3-*ene*.—Thionyl chloride (393 g., 3·3 moles) was added slowly to a stirred ice-cold mixture of *trans*-7-phenylhept-4-en-1-ol [1] (590 g., 3·1 moles), pyridine (1·5 ml.), and benzene (350 ml.). When about one half of the reagent had been added (*ca.* 40 min.), evolution of gas began, after which the remainder was run in quickly without cooling. The mixture was then boiled (caution) until vigorous evolution of gas ceased. It was then cooled and poured on excess of ice, and the organic layer was separated, washed with water, saturated sodium carbonate solution, and brine, dried ($MgSO_4$), and evaporated. Distillation gave trans-7-*chloro*-1-*phenylhept*-3-*ene* (588 g., 91%), b. p. 92—93°/0·3 mm., n_D^{20} 1·5202 (Found: C, 75·2; H, 8·3. $C_{13}H_{17}Cl$ requires C, 74·8; H, 8·2%). The α-*naphthalide* of *trans*-8-phenyloct-5-enoic acid (prepared *via* the Grignard reagent) formed prisms (from methanol), m. p. 113—114° (Found:

[17] Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1939, **61**, 1272.
[18] Olson and Bader, *Org. Synth.*, 1955, **35**, 95.
[19] Schroeder, Stilmar, and Palmer, *J. Amer. Chem. Soc.*, 1956, **78**, 446; cf. Norman and Waters, *J.*, 1956, 2379.

N, 4·1. $C_{24}H_{25}ON$ requires N, 4·1%). Hydrolysis of the Grignard reagent gave trans-1-*phenylhept-3-ene*, b. p. 108—109°/11 mm., n_D^{20} 1·500 (Found: C, 89·6; H, 10·4. $C_{13}H_{18}$ requires C, 89·6; H, 10·4%).

trans-8-*Phenyloct-5-enoic Acid*.—A solution of the Grignard reagent prepared from 7-chloro-1-phenylhept-3-ene (208 g., 1 mole) and magnesium (25·2 g., 1·05 g.-atom) in ether (900 ml.) was poured on a large excess of stirred, finely powdered carbon dioxide and left overnight. Water (750 ml.) and hexane (500 ml.) were then added, followed by sufficient 10N-hydrochloric acid (*ca.* 60 ml.) to give two clear phases. The organic layer was separated and the aqueous phase extracted with hexane (3 × 250 ml.). The combined hexane solutions were extracted with a saturated solution of sodium hydrogen carbonate, and the alkaline solution so obtained back-extracted with hexane and then acidified to Congo-red, at 0°, by stirring it with an equal volume of hexane and cautiously adding 5N-hydrochloric acid. After extraction, etc., as before, distillation gave trans-8-*phenyloct-5-enoic* acid (152 g., 70%), b. p. 134—136°/2 × 10^{-4} mm., n_D^{20} 1·5172 (Found: C, 77·2; H, 8·3. $C_{14}H_{18}O_2$ requires C, 77·0; H, 8·3%). The derived 4-*bromophenacyl ester* (laths from methanol) had m. p. 41—42° (Found: C, 63·4; H, 5·7; Br, 19·4. $C_{22}H_{23}O_3Br$ requires C, 63·6; H, 5·6; Br, 19·2%), and the *phenylhydrazide* (needles from ethanol), m. p. 98—99° (Found: C, 77·5; H, 9·6; N, 8·7. $C_{20}H_{24}ON_2$ requires C, 77·9; H, 7·8; N, 9·1%). Hydrogenation of the acid in the presence of Adams catalyst at room temperature and pressure gave 8-*phenyloctanoic acid* (plates from pentane), m. p. 24—25° (Found: C, 76·3; H, 9·2. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·2%). *trans*-8-Phenyloct-5-enoyl chloride was obtained by the addition of oxalyl chloride (25 g., 0·20 mole) during 15 min. to a warm (50°) stirred solution of the acid (39 g., 0·18 mole) in dry benzene (50 ml.). A stream of dry nitrogen was then passed through the hot solution for 1 hr., after which the solvent was evaporated off and the residue distilled to give *trans*-8-phenyloct-5-enoyl chloride (40 g.), b. p. 85—89°/5 × 10^{-4} mm., n_D^{20} 1·526—1·529. This material slowly resinified and was not obtained pure. Treatment with ammonia gave the *amide* (plates from aqueous ethanol), m. p. 94—95° (Found: C, 77·4; H, 8·7; N, 6·25. $C_{14}H_{19}ON$ requires C, 77·4; H, 8·8; N, 6·45%).

6-1′-*Naphthylhex-3-en-1-ol*.—From 1-bromonaphthalene,[20] 2-1′-naphthylethyl alcohol (88%) was prepared by the entrainment technique [21] and thence 2-1′-naphthylethyl chloride [22] (93%; b. p. 110—112°/0·4 mm., n_D^{20} 1·6182) by the method described above for *trans*-7-chloro-1-phenylhept-3-ene.

A decanted solution of the Grignard reagent prepared from 2-1′-naphthylethyl chloride (231 g., 1·22 moles) and magnesium (1·37 g.-atoms) in ether (700 ml.) was added during 1 hr. to a stirred solution of freshly distilled 2 : 3-dichlorotetrahydrofuran [23] (141 g., 1·0 mole) in ether (300 ml.) so that a steady reflux was maintained. The mixture was stirred until spontaneous refluxing ceased (*ca.* 15 min.), then poured on ice (700 g.) and ammonium chloride (30 g.). On vigorous stirring, two phases separated; the aqueous phase was extracted with ether (2 × 200 ml.). The combined ethereal solutions, which contained 3-chlorotetrahydro-2-(2-1′-naphthylethyl)furan (which decomposed on distillation and therefore was not isolated), were dried ($MgSO_4$; $CaSO_4$) and added to a stirred suspension of sodium sand [(51 g., 2·2 g.-atoms) in ether (150 ml.)] [the reaction having been initiated by the addition of tetrahydrofurfuryl chloride (1 ml.) so that controlled spontaneous reflux was maintained. When the addition was complete (*ca.* 1 hr.) the mixture was stirred for a further hour at room temperature. Sufficient water (*ca.* 500 ml.) (caution) was added to give two phases which were separated and the aqueous phase was extracted with ether. Distillation of the dried ($MgSO_4$) combined extracts gave, after elimination of low-boiling material, *cis* + *trans*-6-1′-naphthylhex-3-en-1-ol (83 g., 37% based on dichlorotetrahydrofuran), b. p. 145—55°/3 × 10^{-3} mm., n_D^{16} 1·591—1·593 (Found: C, 84·0; H, 8·5. Calc. for $C_{16}H_{18}O$: C, 84·9; H, 8·0%).

cis + trans-7-1′-*Naphthylhept-4-enoic Acid*.—Conversion of the above alkenol (69 g.) into the chloride (70 g.; b. p. 135—145°/6 × 10^{-3} mm., n_D^{16} 1·587—1·592) and carboxylation of the Grignard reagent were carried out as for *trans*-8-phenyloct-5-enoic acid. The crude acid (30 g.) was a viscous oil, which slowly deposited crystals; after two years these were collected (8·7 g.) and crystallised from hexane, to give *trans*-7-1′-naphthylhept-4-enoic acid, whose m. p. (65—69°) was not depressed on admixture with the acid prepared from *trans*-7-1′-naphthylhept-4-en-1-ol.

[20] Merz and Weith, *Ber.*, 1882, **15**, 2708.
[21] Bachmann, Cole, and Wilds, *J. Amer. Chem. Soc.*, 1940, **62**, 824; Wilds and Close, *ibid.*, 1947, **69**, 3079.
[22] Cf. Cook and Hewett, *J.*, 1933, 1098.
[23] Crombie and Harper, *J.*, 1950, 1707, 1714.

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trans-7-1′-*Naphthylhept*-4-*en*-1-*ol*.—This *alkenol*, b. p. 165—68°/0·8 mm., n_D^{20} 1·579—1·581 (Found: C, 84·3; H, 8·4. $C_{17}H_{26}O$ requires C, 84·9; H, 8·4%), was prepared (57% yield) by ring scission of the crude product of the coupling of 2-1′-naphthylethylmagnesium chloride (1·78 moles) and 2 : 3-dichlorotetrahydropyran [23] (1·42 moles) as described for the above naphthylhexenol.

Oxidation of trans-7-1′-*Naphthylhept*-4-*en*-1-*ol*.—Chromium trioxide (65 g., 0·62 mole) was added with stirring during 40 min. to pure pyridine (650 ml.), at 25°, the internal temperature being maintained at this value by intermittent cooling. The mixture was stirred at room temperature for 30 min. after which *trans*-7-1′-naphthylhept-4-en-1-ol (65 g., 0·27 mole) was added and stirring continued for 16 hr. After dilution with ice-water (1·5 l.) the solution was extracted with ether (3 × 1 l.), and these extracts were washed with water (2 × 500 ml.) and 0·5N-potassium hydroxide (2 × 250 ml.). Evaporation of the ethereal extracts and desiccation of the residual oil gave crude *trans*-7-1′-naphthylhept-4-enal (49 g., 76%). The derived 2 : 4-*dinitrophenylhydrazone* (yellow needles from ethanol) had m. p. 145—146° (Found: C, 66·4; H, 5·3; N, 13·0. $C_{23}H_{28}O_4N_4$ requires C, 66·0; H, 5·3; N, 13·4%).

The alkaline washings were extracted with ether and then acidified to Congo-red with 2N-hydrochloric acid. The red precipitate was extracted with benzene (2 × 100 ml.), the extract evaporated, and the residue neutralised with N-ammonia. The resulting solution was treated with a cold saturated aqueous solution of *S*-benzylthiuronium chloride (6·0 g.), and the precipitate was recrystallised from ethanol, to yield S-*benzylthiuronium* trans-7-1′-*naphthylhept*-5-*enoate* (10·5 g., 9·2%) as laths, m. p. 162—166°. A sample recrystallised twice more had m. p. 166—167° (Found: C, 71·1; H, 6·4; N, 6·9. $C_{25}H_{28}O_2N_2S$ requires C, 71·4; H, 6·7; N, 6·7%). The salt (10 g.) was shaken with ice-cold N-hydrochloric acid (25 ml.) and ether (25 ml.). Material from the ethereal layer yielded trans-7-1′-*naphthylhept*-4-*enoic acid* (5·9 g.), m. p. 67—69° (from hexane). Two further recrystallisations (in the presence of fuller's earth) gave the pure acid as prisms, m. p. 69—70° (Found: C, 80·3; H, 7·35. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·15%).

The above crude *trans*-7-1′-naphthylhept-4-en-al (49 g., 0·20 mole) was added to a stirred suspension of dry freshly prepared silver oxide (58 g., 0·25 mole) in benzene (100 ml.). At 65°, an exothermic reaction set in and silver was deposited. After 30 minutes' stirring under reflux the mixture was cooled in ice, treated with 2N-nitric acid (200 ml.), and centrifuged to give a clear benzene layer, from which was obtained, *via* the *S*-benzylthiuronium salt as above, *trans*-7-1′-naphthylhept-5-enoic acid (8·3 g., 12%), m. p. 67—69°.

The derived *acid chloride*, prepared as for 8-phenyloct-5-enoyl chloride, had b. p. 165—168°/2 × 10^{-2} mm., n_D^{21} 1·5828 (Found: C, 75·7; H, 6·5; Cl, 12·1. $C_{17}H_{17}OCl$ requires C, 74·8; H, 6·3; Cl, 13·0%), and the *amide* (plates from aqueous ethanol) had m. p. 84—85° (Found: N, 5·9. $C_{17}H_{19}ON$ requires N, 5·5%).

Cyclisation of trans-8-*Phenyloct*-5-*enoic Acid*.—This acid (30 g.) was treated with polyphosphoric acid [24] (300 g.) at 110° for 2 hr., in an atmosphere of nitrogen as previously described.[2] Distillation of the oil obtained on evaporation of the ethereal extract gave 1 : 2 : 3 : 7 : 8 : 9 : 10 : 10*a*-octahydro-7-oxo*cyclo*hepta[*de*]naphthalene (20 g., 73%), b. p. 135—145°/0·5 mm., m. p. 60—63° (pale yellow). Recrystallisation from methanol yielded off-white plates, m. p. 63—64° (Found: C, 83·6; H, 8·6. Calc. for $C_{14}H_{16}O$: C, 83·95; H, 8·1%), $\lambda_{max.}$ 252 and 291, $\lambda_{min.}$ 230 and 278 mμ (log ε 3·88, 3·22, 3·33, and 3·10 respectively). The derived oxime (plates from aqueous ethanol) had m. p. 162—163°; the semicarbazone (from methanol) had m. p. 215—216° (decomp.) (Found: N, 16·3. Calc. for $C_{15}H_{19}ON_3$: N, 16·3%); and the 2 : 4-dinitrophenylhydrazone (orange laths from ethanol–chloroform) had m. p. 187—188° (Found: C, 63·2; H, 5·4; N, 14·7. Calc. for $C_{20}H_{20}O_4N_4$: C, 63·1; H, 5·3; N, 14·7%). The reported constants for this ketone are m. p. 63° (ref. 25) and 61·5—63° (ref. 5); semicarbazone, m. p. 221° (ref. 25); 2 : 4-dinitrophenylhydrazone (yellow), m. p. 162—165° (ref. 5). Reduction of the ketone with lithium aluminium hydride in ether gave the 7-hydroxy-compound (tablets from ethyl acetate–hexane), m. p. 87—89° (lit.,[26] m. p. 93—94°), dehydrogenation of which with palladised charcoal gave 7 : 8 : 9 : 10-tetrahydro*cyclo*hepta[*de*]naphthalene (plates from methanol), m. p. 57—58° (lit.,[27] m. p. 57—58°) [picrate (orange needles from

[24] Uhlig, *Angew. Chem.*, 1954, **66**, 325.
[25] von Braun and Rath, *Ber.*, 1927, **60**, 1182.
[26] Gardner and Horton, *J. Amer. Chem. Soc.*, 1952, **74**, 657.
[27] Boekelheide and Vick, *ibid.*, 1956, **78**, 653.

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ethanol), m. p. 115—117°; styphnate (yellow needles from ethanol), m. p. 119—121° (lit.,[5] m. p. 114—115·5° and 118·5—121° respectively). The *trinitrobenzene complex* (golden needles from ethanol) had m. p. 138—139° (Found: N, 10·2. $C_{20}H_{21}O_6N_3$ requires N, 10·6%).

Cyclisation of trans-8-*Phenyloct-5-enoyl Chloride*.—The acid chloride (41 g.) was cyclised as previously described,[2] but under nitrogen. The crude product from the carbon disulphide extract gave material (15 g.) of b. p. 155—158°/1 mm., n 1·559—1·567, containing only a trace of chlorine. This was fractionally distilled at 3·5 mm. (100 × 0·6 cm. spinning-band fractionating column from E. Haage, Mülheim) to yield fractions: (1) b. p. <130°, n_D^{20} 1·556 (0·3 g.); (2) b. p. 130—147°, n_D^{20} 1·550 (0·5 g.); (3) b. p. 147—150°, n_D^{20} 1·552 (0·5 g.); and (4) b. p. 150—150·5° (5·5 g.), m. p. 63—72°. From fraction (1) was prepared a 2 : 4-dinitrophenylhydrazone (red needles from benzene–ethanol), m. p. 266—267° (Found: N, 15·3. Calc. for $C_{20}H_{20}O_4N_4$: N, 14·7%) (not 2-phenethyl*cyclo*hex-2-enone 2 : 4-dinitrophenylhydrazone,[28] m. p. 155—157°). Fractions (2) and (3) yielded only complex mixtures of yellow and red 2 : 4-dinitrophenylhydrazones. The semicarbazones of fraction (3) were separated by fractional crystallisation into prisms, m. p. 203—204° (Found: C, 70·6; H, 7·5; N, 16·3. Calc for $C_{15}H_{19}ON_3$: C, 70·0; H, 7·45; N, 16·3%) (which could be converted into a yellow 2 : 4-dinitrophenylhydrazone), and tablets whose m. p. 216—218° was not depressed in admixture with the semicarbazone of fraction (4). Recrystallisation of fraction (4) from methanol yield 1 : 2 : 3 : 4 : 4*a* : 9 : 10 : 10*a*-*octahydro*-1-*oxophenanthrene* as prisms, m. p. 76—77° (Found: C, 83·7; H, 8·0. $C_{14}H_{16}O$ requires C, 83·95; H, 8·1%), $\lambda_{max.}$ 265 and 272, $\lambda_{min.}$ 241 mμ (log ε 1·79, 1·81, 1·38, 1·56 respectively). The *oxime* (needles from aqueous ethanol) had m. p. 184—186° (Found: C, 77·8; H, 7·8; N, 6·6. $C_{14}H_{17}ON$ requires C, 78·1; H, 8·0; N, 6·5%); the *semicarbazone* (phototropic tablets from ethanol) had m. p. 218—219° (Found: C, 70·1; H, 7·6; N, 16·0. $C_{15}H_{19}ON_3$ requires C, 70·0; H, 7·45; N, 16·3%); and the 2 : 4-*dinitrophenylhydrazone* (yellow plates from ethanol–chloroform) had m. p. 221—224° (Found: C, 62·7; H, 5·5; N, 15·3. $C_{20}H_{20}O_4N_4$ requires C, 63·1; H, 5·3; N, 14·7%).

The above ketone (1·2 g.) in ether (25 ml.) was added to the reagent from methyl iodide (3·5 g.) and magnesium (0·45 g.) in ether (50 ml.). The mixture was boiled under reflux for 4 hr., then cooled and treated with a cold saturated aqueous solution of ammonium chloride (2 g.). Evaporation of the dried (K_2CO_3) ethereal extract yielded an oil (giving no precipitate with Brady's reagent), which was heated with 5% palladised charcoal (1 g.) at 310° in nitrogen for 5 hr. The mixture was extracted with boiling ethanol, and the extract then evaporated to yield 1-methylphenanthrene (0·6 g.), m. p. 119—120° (lit.,[29] m. p. 118—119°). The picrate, styphnate, and 1 : 3 : 5-trinitrobenzene complex had m. p. 135—137°, 153—154°, and 158—159° respectively (lit.,[29] 135·5—137°, 150·5—152°, and 160—161° respectively).

Cyclisation of trans-7-1′-*Naphthylhept*-4-*enoic Acid*.—This acid (2·0 g.) was treated with polyphosphoric acid (20 g.) at 90°, in nitrogen, as previously described. The mixture rapidly became homogeneous and after 5 min. was poured into water. Evaporation of the neutral ethereal extract and recrystallisation of the residue (from ethanol) gave pale yellow 1 : 2 : 3 : 3*a* : 4 : 5-*hexahydrobenz*[de]*anthr*-6-*one* (1·3 g., 70%), m. p. 123—125°. The analytical sample (off-white needles) had m. p. 124—125° (Found: C, 86·2; H, 6·80. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%), $\lambda_{max.}$ 296, 307, 353, $\lambda_{min.}$ 270, 302, and 325 mμ (log ε 2·93, 2·92, 2·38, 2·45, 2·85, and 2·14 respectively). The oxime had m. p. 192—193° (decomp.), and the 2 : 4-dinitrophenylhydrazone m. p. 293—294° (decomp.). The m. p.s of the ketone and its derivatives were not depressed on admixture with authentic samples (see below).

β-(1 : 2 : 3 : 4-*Tetrahydro*-1-*phenanthryl*)*propionic Acid*.—β-(3 : 4-Dihydro-1-phenanthryl)-propionic acid [14] (1·5 g.) was hydrogenated in the presence of Adams catalyst (0·1 g.) in ethyl acetate (50 ml.) at atmospheric pressure and room temperature. After removal of the catalyst the solution was concentrated to *ca.* 5 ml. and cooled, depositing crystals which were filtered off and dried to yield β-(1 : 2 : 3 : 4-tetrahydro-1-phenanthryl)propionic acid (1·4 g., 93%), plates, m. p. 146—147° (from ethyl acetate) (Found: C, 79·7; H, 7·5. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·15%). Hoch [13] records m. p. 115°. The S-*benzylthiuronium* salt (tablets from ethanol) had m. p. 158—159° (Found: N, 6·9; S, 7·4. $C_{22}H_{26}O_2N_2S$ requires N, 6·7; S, 7·6%).

1 : 2 : 3 : 3*a* : 4 : 5-*Hexahydrobenz*[de]*anthr*-6-*one*.—The tetrahydrophenanthrylpropionic acid (1·0 g.) was treated with polyphosphoric acid (20 g.) at 95° in nitrogen as previously described and was poured into water after 50 min. Evaporation of the neutral ethereal extract left a

[28] Ansell and Ducker, unpublished work.
[29] Adkins and England, *J. Amer. Chem. Soc.*, 1949, **71**, 2958.

bright yellow solid (0·9 g.), m. p. 119—122°, which on repeated recrystallisation from methanol gave the ketone with the m. p. and spectrum recorded above (Found: C, 85·6; H, 7·3%). The *oxime* (tablets from ethanol) had m. p. 191—192° (decomp.) (Found: N, 5·5. $C_{17}H_{17}ON$ requires N, 5·6%), and the 2 : 4-*dinitrophenylhydrazone* (red rhombs from chloroform) had m. p. 291—292° (decomp.) (Found: C, 65·9; H, 4·7. $C_{23}H_{20}O_4N_4$ requires C, 66·3; H, 4·8%).

Attempted Cyclisation of trans-7-1′-*Naphthylhept*-4-*enoyl Chloride.*—Cyclisation of this acid chloride (2·0 g.) as previously described [2] gave tar. Heating for only 35 min. yielded material, from the methanolic extract of which was prepared a 2 : 4-dinitrophenylhydrazone [of 2-(2-1′-naphthylethyl)*cyclo*pent-2-enone(?) (red needles from chloroform), m. p. 228—229° (Found: N, 13·2. Calc. for $C_{23}H_{20}O_4N_4$: N, 13·5%)]. At lower reaction temperatures (−10° to +20°) no ketone was isolated; at −10°, some unchanged acid chloride was recovered.

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801. *Isomerisation of Phenylpropargylidenemalonic Acid to γ-Benzylidene-α-carboxybutenolide.*

By JUAN CASTAÑER and JOSÉ PASCUAL.

Phenylpropargylidenemalonic acid is converted into γ-benzylidene-α-carboxybutenolide by thermal isomerisation as well as through the silver salt. The structure of the product has been established by spectral and chemical evidence.

THE product of reaction of phenylpropargylaldehyde and malonic acid in acetic acid has been shown to be phenylpropargylidenemalonic acid (I; R = H).[1,2] The present work describes some properties of this substance.

The melting point 218° of this acid corresponds to that of an isomer formed during the heating (about 150—170°) and shown to be γ-benzylidene-α-carboxybutenolide * (II; R = CO_2H) by the following evidence:

(I) (II)

The acid (II; R = CO_2H), through its silver salt, gave a methyl ester (II; R = CO_2Me), which with hydrochloric acid in dioxan regenerated the acid (II; R = CO_2H). When this acid was heated at 250° *in vacuo* it yielded γ-benzylidenebutenolide (II; R = H), first prepared by H. Gilman and his co-workers.[3] Catalytic hydrogenation of the acid (II; R = CO_2H), followed by decarboxylation of the resulting gum, furnished a mixture from which were isolated δ-phenyl-*n*-valeric acid and γ-benzylbutanolide, characterised as γ-hydroxy-δ-phenyl-*n*-valero-*p*-toluidide and by reduction with hydriodic acid to δ-phenyl-*n*-valeric acid.

The ultraviolet spectra of compounds (I; R = H) $\lambda_{max.}$ 312 mμ (ε 20,000), (I; R = Me) [1]

* Jacobs and his co-workers' assumption that the isomerisation product of m. p. 218° is 6-phenyl-α-pyrone-3-carboxylic acid is untenable because this substance has already been reported with different properties.[1]

[1] Castañer and Pascual, *Anales real. Soc. Espan. Fis. Quim.*, 1957, **53**, *B*, 651.
[2] Jacobs, Dankner, and Dankner, *J. Amer. Chem. Soc.*, 1958, **80**, 864.
[3] Gilman, Franz, Hewlett, and Wright, *J. Amer. Chem. Soc.*, 1950, **72**, 3.

$\lambda_{max.}$ 316 mμ (ε 22,500), (II; R = H) $\lambda_{max.}$ 331 mμ (ε 26,050), (II; R = CO_2H) $\lambda_{max.}$ 358 mμ (ε 35,890), and (II; R = CO_2Me) $\lambda_{max.}$ 361 mμ (ε 29,270) are in good agreement with the accepted conjugation of the unsaturated bonds [4] and with the bathochromic effect due to cyclisation.[5]

In the infrared spectra of these substances and of phenylpropargylaldehyde (A) there are acetylenic bands at 2233—2183 (A), 2183 (I; R = H), and 2199 $cm.^{-1}$ (I; R = Me), that have disappeared in the spectra of the lactones (II). There are also bands at 1790 and 1750 $cm.^{-1}$ for the lactones (only a shoulder for II, R = CO_2H), that must be due to the γ-ylidenebut-αβ-enolide system (cf. the double band in Fig. 2 of ref. 6).

Addition of aqueous silver nitrate to an alcoholic solution of the acid (I; R = H) gave a precipitate which, on treatment with hydrogen sulphide afforded acid (II; R = CO_2H), and with methyl iodide gave the methyl ester (II; R = CO_2Me). The dimethyl ester (I; R = Me) was, however, obtained by treating the acid (I; R = H) with the theoretical amount of diazomethane.[1]

The acid (I; R = H) is probably also partially isomerised by alkali since the correct equivalent weight is obtained only from acid prepared in the cold and then only by titration (with sodium hydroxide) in the cold (cf. refs. 1 and 2).

The transformation:

is a nucleophilic addition of the carbonyloxy-group to the triple bond, and the resulting butenolide probably has a *trans*-ylidene bond. Recently, the same lactonisation, effected however under different conditions, has been reported in the polyacetylenic acid series.[6,7]

Experimental

γ-Benzylidene-α-carboxybutenolide.—(*a*) Phenylpropargylidenemalonic acid (30 g.) was heated at 190° for 10—15 min. After cooling the product was washed with benzene. Recrystallisation from dioxan gave *γ-benzylidene-α-carboxybutenolide* (27 g.), as yellow rhombs, m. p. 218° (decomp.) (Found: C, 66·6; H, 3·8. $C_{12}H_8O_4$ requires C, 66·7; H, 3·7%).

(*b*) Silver nitrate (0·8 g.) in water (10 c.c.) was added to phenylpropargylidenemalonic acid (0·4 g.) in alcohol (6 c.c.). A brown precipitate appeared. More water (16 c.c.) was added. The precipitate became yellow after a few minutes and then was collected, suspended in water, and treated with hydrogen sulphide. The silver sulphide and free acid were filtered off and extracted with boiling dioxan. The yellow solution was concentrated to a small volume and water was added. The yellow precipitate was recrystallised from dioxan, to give γ-benzylidene-α-carboxybutenolide (0·35 g.) as yellow rhombs, m. p. 218° (decomp.).

γ-Benzylidene-α-methoxycarbonylbutenolide.—γ-Benzylidene-α-carboxybutenolide (1 g.) was treated with silver nitrate as above. The precipitate was collected and dried. The dry salt was ground and shaken for 24 hr. with methyl iodide. The precipitated silver iodide was filtered off and the solution was evaporated to dryness. Recrystallisation of the residue from ether gave the *ester* (0·72 g.), as yellow needles with a weak green fluorescence, m. p. 151—153° (Found: C, 67·9; H, 4·4. $C_{13}H_{10}O_4$ requires C, 67·8; H, 4·4%).

Phenylpropargylidenemalonic acid treated as above gave the same compound, m. p. 151—153°.

A solution of γ-benzylidene-α-methoxycarbonylbutenolide (0·2 g.) in dioxan (6 c.c.) and concentrated hydrochloric acid (8 c.c.) was refluxed for 5 hr. After cooling, more water (14 c.c.)

[4] Houben-Weyl, "Methoden der Organischen Chemie," Georg Thieme Verlag, Stuttgart, 1955, Vol. B III, Part 2, p. 654.
[5] Braude and Nachod, "Determination of Organic Structures by Physical Methods," Academic Press Inc., New York, 1955, p. 154.
[6] Christensen, Sorensen, Bell, Jones, and Whiting, "Festschrift Arthur Stoll," Basel, 1957, p. 545.
[7] Bell, Jones, and Whiting, *J.*, 1958, 1313.

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was added, whereupon a yellow precipitate was formed, which was collected and recrystallised from dioxan to give γ-benzylidene-α-carboxybutenolide, m. p. 218° (decomp.).

γ-Benzylidenebutenolide.—γ-Benzylidene-α-carboxybutenolide (3 g.) was heated *in vacuo* at 240—250°. A yellow oil, that solidified easily, distilled at 180°. This yellow solid recrystallised from ether to give γ-benzylidenebutenolide [3] (1·2 g.) as white prisms, m. p. 86—87° (Found: C, 76·6; H, 4·55. Calc. for $C_{11}H_8O_2$: C, 76·7; H, 4·7%), whose structure was confirmed by reduction with hydriodic acid to δ-phenyl-lævulic acid, as indicated by Gilman.[3]

Catalytic Hydrogenation of γ-Benzylidene-α-carboxybutenolide.—γ-Benzylidene-α-carboxybutenolide (4 g.) in alcohol (200 c.c.) was hydrogenated over Adams catalyst (0·15 g.) at 1 atm. (absorption 865 c.c.; theor., 861 c.c.). After filtration and evaporation the residue was a yellowish gum (3·95 g.) which was heated *in vacuo* at 140—150° for 15 min., then extracted with aqueous sodium hydroxide. The alkaline solution was acidified with hydrochloric acid and extracted with ether. Evaporation of the dried ethereal solution gave an oil which partially crystallised. Filtration of this material afforded a solid A (0·25 g.) and an oil B (1·6 g.). The solid A (0·25 g.), recrystallised from ether, gave δ-phenyl-*n*-valeric acid (0·20 g.), m. p. and mixed m. p. 58—59°. The liquid B (1·5 g.) in ether (20 c.c.) was added to a Grignard reagent prepared by adding *p*-toluidine to ethereal ethylmagnesium bromide. After 30 minutes' refluxing more ether (50 c.c.) was added and the cold solution was washed several times with 2N-hydrochloric acid, then with water. The dried ethereal solution was evaporated and the residue recrystallised from ether, to give *γ-hydroxy-δ-phenyl*-n-*valero*-p-*toluidide* (1·6 g.) as needles, m. p. 144—145° (Found: C, 76·15; H, 7·5; N, 5·0. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·5; N, 4·9%).

The liquid B (1 g.), acetic acid (20 c.c.), and 40% hydriodic acid (20 c.c.) were heated at 160° during 6 hr. in a sealed tube, then diluted with water (100 c.c.), decolorised with a few drops of sodium hydrogen sulphite solution, and extracted with ether. The ethereal solution was extracted with aqueous sodium carbonate. The alkaline solution was acidified with hydrochloric acid and extracted with ether. This extract was dried and evaporated *in vacuo*. The residue, recrystallised from ether, gave δ-phenyl-*n*-valeric acid (0·8 g.), needles, m. p. 58—59°.

Titration of Phenylpropargylidenemalonic Acid.—The acid (11·06 mg.), prepared without heating,[1] was titrated in the cold (5·26 c.c. of 0·0196N-sodium hydroxide; equivalent, 107·3. Calc., 108·1). If the titration was carried out hot, or if heat was used in preparation of the acid, the values were about 120.

We are grateful to Dr. J. Morcillo who determined and interpreted the infrared spectra and to Dr. J. Estevan and his assistants who made the analyses. One of us (C. J.) is indebted for a Research Fellowship of the " Fundación Juan March " during 1957.

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802. *Infrared Spectra of Uranyl Nitrate Hydrates and Rubidium Uranyl Nitrate.*

By Bryan M. Gatehouse and Alan E. Comyns.

The infrared spectra of uranyl nitrate di-, tri-, and hexa-hydrate have been examined from 3700 to 700 cm.$^{-1}$, with nitrogen of normal isotopic composition and enriched in ^{15}N, and most of the bands are assigned.

The spectrum of uranyl nitrate hexahydrate is in most respects that of a typical ionic nitrate.

The spectra of uranyl nitrate di- and tri-hydrate are similar to the spectrum of rubidium uranyl nitrate, and all three are closely related to the fluorescence spectrum of cæsium uranyl nitrate, studied by Dieke and Duncan. These spectra are all characteristic of compounds having co-ordinated nitrato-groups, and structures are suggested for the molecules in crystals of the di- and the tri-hydrate which account for the observed splitting of many of the bands.

There have been several investigations of the infrared spectra of the hydrates of uranyl nitrate,[1-5] but there has been no detailed assignment of the bands. The infrared spectrum of rubidium uranyl nitrate has not hitherto been reported.

Sevchenko and Stepanov [2] examined the spectrum of the hexahydrate and, without reference to the frequencies expected to arise from the nitrate ion, assigned all the peaks in the region 870—2000 cm.$^{-1}$ to combinations or overtones of the three fundamental frequencies of the uranyl ion. They also reported the synthesis of uranyl nitrate tri-, di-, and mono-hydrate and the anhydrous compound and gave their spectra, observing that the band at 1390 cm.$^{-1}$ occurs strongly only in the hexahydrate. Although Sevchenko and Stepanov stated that the compositions of the hydrates had been established by analysis, the preparations were not described and the existence of a monohydrate and an anhydrous phase in this system is not generally recognised.[6] Burger and Moore [4] tabulated the frequencies in the infrared spectrum of uranyl nitrate dihydrate, both for the solid state and for solutions in organic solvents: they assigned the frequencies to vibrations of uranyl and nitrate ions, but without specifying the vibrations. Tridot [5] examined the spectra of the di-, tri-, and hexa-hydrate suspended in carbon tetrachloride and found them to vary markedly with the state of hydration.

Previous work on the fluorescence,[7,8,9] infrared,[1,2,10,11] and Raman [10,12,13,14] spectra of uranyl compounds, both in the solid state and in solution, has established that the uranyl ion has three fundamental vibration frequencies: *A* (860 cm.$^{-1}$, symmetrical stretching), *B* (930 cm.$^{-1}$, antisymmetric stretching), and *C* (210 cm.$^{-1}$, bending). The only frequency normally observed in the infrared spectrum is *B*, since *A* is forbidden for a linear ion and *C* is outside the usual spectral range. However, frequency *A* is sometimes observed weakly in the infrared spectrum and the reasons for this have been discussed by Crandall [13] and by Sutton.[14]

[1] Lecomte and Freymann, *Bull. Soc. chim. France*, 1941, **8**, 622.
[2] Sevchenko and Stepanov, *Zhur. eksp. teor. Fiz.*, 1949, **19**, 1113 (A.E.R.E. Translation No. 11/3/5/80).
[3] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 309.
[4] Burger and Moore, U.S.A.E.C. document HW-18260 (1950).
[5] Tridot, *Ann. Chim.* (*France*), 1955, **10**, 225.
[6] Katz and Seaborg, "The Chemistry of the Actinide Elements," Methuen, London, 1957, p. 193.
[7] Nichols and Howes, "Fluorescence of the Uranyl Salts," Carnegie Inst. Wash. publ. no. 298 (1919).
[8] Freymann, *J. Phys. Radium*, 1948, **9**, 158.
[9] Dieke and Duncan, "Spectroscopic Properties of Uranium Compounds," McGraw-Hill, New York, 1949, pp. 36 *et seq.*
[10] Conn and Wu, *Trans. Faraday Soc.*, 1938, **34**, 1483.
[11] Jones, *J. Chem. Phys.*, 1955, **23**, 2105.
[12] Satyanarayana, *Proc. Indian Acad. Sci.*, 1942, **15**, *A*, 414.
[13] Crandall, *J. Chem. Phys.*, 1949, **17**, 602.
[14] Sutton, A.E.R.E. C/R 769 (1951); *Nature*, 1952, **169**, 235.

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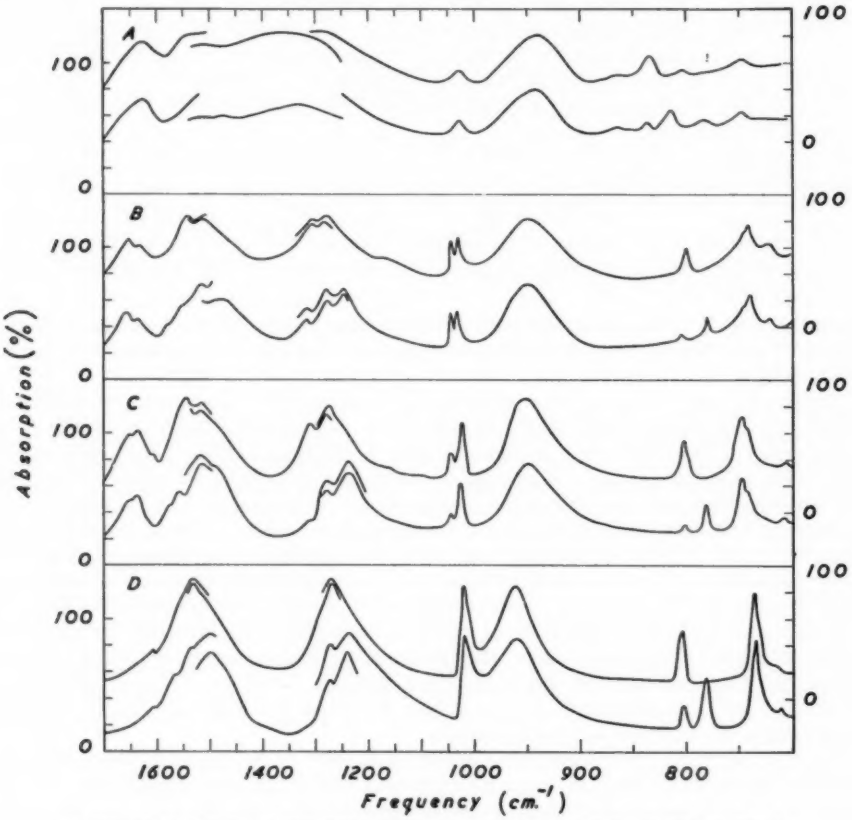
The fluorescence and visible absorption spectra of rubidium and cæsium uranyl nitrate were studied in great detail by workers for the American Atomic Energy Project,[9] and the hydrates of uranyl nitrate were studied to a smaller extent. The fine structures of these



A, $UO_2(NO_3)_2,6H_2O$; *B*, $UO_2(NO_3)_2,3H_2O$; *C*, $UO_2(NO_3)_2,2H_2O$; *D*, $RbUO_2(NO_3)_3$.

Upper curves (ordinate scales at right-hand side) refer to compounds of normal isotopic composition; lower curves (ordinate scales at left-hand side) refer to compounds enriched in ^{15}N. *Regions* 1200—1500 *cm.*$^{-1}$ *are for hexachlorobutadiene suspensions, other regions for Nujol suspensions.*

spectra are closely related to the infrared spectra, but the latter were not studied by these workers.

The only crystallographic work on these compounds has been by Pauling and Dickinson [15] who located the uranium atoms in the unit cell of uranyl nitrate hexahydrate, and by Hoard and Stroupe [16] who obtained a fairly detailed picture of the structure of rubidium uranyl nitrate.

Recent work [17] on the infrared spectra of a series of nitratocobaltammines has enabled the vibration frequencies of the co-ordinated nitrato-group to be assigned and to be distinguished from those of the nitrate ion; with these results as a guide we have re-examined the uranyl nitrate spectra.

[15] Pauling and Dickinson, *J. Amer. Chem. Soc.*, 1924, **46**, 1615.
[16] Hoard and Stroupe, ref. 9, pp. 13 *et seq.*
[17] Gatehouse, Livingstone, and Nyholm, *J.*, 1957, 4222.

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Experimental

Materials.—Uranyl nitrate hexahydrate (" AnalaR ") was recrystallised from water and analysed by ignition to U_3O_8 at 750—800° [Found: U, 47·32, 47·26. Calc. for $UO_2(NO_3)_2,6H_2O$: U, 47·42%].

Uranyl nitrate trihydrate was prepared [18] by storing the powdered hexahydrate over sulphuric acid (*d* 1·54) *in vacuo* for 4 weeks; after 2 weeks the acid was renewed and the sample ground and replaced [Found: U, 53·24, 53·30. Calc. for $UO_2(NO_3)_2,3H_2O$: U, 53·12%]. The trihydrate was also prepared [19] in the form of large crystals by evaporating a solution of the hexahydrate in nitric acid (*d* 1·4) over solid potassium hydroxide.

Uranyl nitrate dihydrate was prepared similarly to the trihydrate (first method), but by using concentrated sulphuric acid (*d* 1·84) [Found: U, 55·41, 55·48. Calc. for $UO_2(NO_3)_2,2H_2O$: U, 55·35%]. Attempts to crystallise the dihydrate [19] from a solution of anhydrous uranium trioxide in fuming nitric acid (*d* 1·5) were unsuccessful: microscopic examination showed the crystals to be of the trihydrate.

Rubidium uranyl nitrate was prepared by dissolving rubidium nitrate (1·0 g.) and uranyl nitrate hexahydrate (3·4 g.) in separate portions of concentrated nitric acid (2 ml. and 3·5 ml. respectively) and mixing the warm solutions. Crystallisation started almost immediately and the crystals were filtered off from the warm solution. The product was dried in a vacuum-desiccator over sodium hydroxide (yield 2·5 g.) and analysed by precipitation as ammonium diuranate and ignition to U_3O_8 [Found: U, 44·53, 44·18. Calc. for $RbUO_2(NO_3)_3$: U, 43·95%].

The same compounds, enriched in ^{15}N, were prepared by similar methods from a sample of enriched nitric acid. They were not analysed, but the similarities of their spectra to those of the isotopically normal compounds, together with their methods of preparation, establish their identities. The isotopic composition of the nitric acid was not measured directly: instead, the rubidium uranyl nitrate prepared from it was decomposed thermally and the resulting oxides of nitrogen were reduced to nitrogen by iron powder. Mass-spectrographic analysis of this nitrogen showed it to contain 81·9 atoms % of ^{15}N.

Spectra.—A Grubb–Parsons double-beam infrared spectrometer was used, equipped with an S3A monochromator and a sodium chloride prism. The samples were examined as suspensions in Nujol and, for the 1200—1500 cm.$^{-1}$ region, as suspensions in hexachlorobutadiene. The cell windows were of sodium chloride coated with polystyrene: use of coated windows has been found to be essential for work on nitrates,[17,20] since some compounds with co-ordinated nitrato-groups react with sodium chloride windows and the products give the spectrum of the nitrate ion. The reaction with uncoated windows was observed in preliminary work with uranyl nitrate tri- and hexa-hydrate, but not with the dihydrate or rubidium uranyl nitrate. The spectrum of rubidium uranyl nitrate from 700 to 400 cm.$^{-1}$ was recorded by using a Hilger double-beam spectrophotometer, model H 800, equipped with a cæsium bromide prism.

Results and Discussion

The spectra of rubidium uranyl nitrate and uranyl nitrate di- and tri-hydrate are closely related and will be discussed together. The spectrum of uranyl nitrate hexahydrate is in most respects that of an ionic nitrate. They are illustrated in the Figure.

In all the spectra the frequencies of the *B* vibration of the uranyl ion (antisymmetric stretching) are close to those reported by others,[1-5,8-11] and the *A* vibration (symmetric stretching), forbidden in the infrared for the free ion, was observed only in the spectrum of uranyl nitrate hexahydrate.

Conventions for numbering the vibrations of the nitrate ion [21] differ from those used for the nitrato-group (*e.g.*, in nitric acid,[22,23] methyl nitrate,[24] and nitrato-co-ordination complexes [17]). To avoid confusion, since the convention for the nitrate ion is here

[18] Katzin, Simon, and Ferraro, *J. Amer. Chem. Soc.*, 1952, **74**, 1191.
[19] Ref. 7, p. 208.
[20] Gatehouse, *Chem. and Ind.*, 1957, 1351.
[21] Herzberg, " Infra-red and Raman Spectra of Complex Molecules," Van Nostrand, New York, 1945, p. 179.
[22] Redlich and Nielsen, *J. Amer. Chem. Soc.*, 1943, **65**, 654.
[23] Ingold and Millen, *J.*, 1950, 2612; Cohn, Ingold, and Poole, *J.*, 1952, 4272.
[24] Brand and Cawthon, *J. Amer. Chem. Soc.*, 1955, **77**, 319.

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employed to describe the spectrum of uranyl nitrate hexahydrate, whereas that for the nitrato-group is used for all the other spectra, the relations between these two sets of conventions are shown in Table 1. The symmetry types of the vibrations are given in

TABLE 1.

NO_3^-	ν_1 (A_1') NO stretch.	ν_2 (A_2'') Out of plane	ν_3 (E') NO_2 stretch.		ν_4 (E') NO_2 bend.	
O_2NO	ν_2 (A_1) NO stretch.	ν_6 (B_2) Out of plane	ν_1 (A_1) NO_2 stretch. symmetric	ν_4 (B_1) NO_2 stretch. antisymmetric	ν_3 (A_1) NO_2 bend. symmetric	ν_5 (B_1) NO_2 bend. antisymmetric

parentheses; their approximate forms have been illustrated by, *inter al.*, Redlich and Nielsen [22] and by Cohn, Ingold, and Poole.[23]

The fundamentals in the infrared spectra of rubidium uranyl nitrate and of uranyl nitrate di- and tri-hydrate are given in Table 2, together with the frequencies in the fluorescence spectrum of cæsium uranyl nitrate which Dieke and Duncan recognised, from their nitrogen-isotope shifts, as arising from vibrations of the nitrate ion but could not assign in detail.

Nitric acid and methyl nitrate have bands in the Raman spectrum at 680 and 610 cm.$^{-1}$, and 664 and 578 cm.$^{-1}$ respectively; but whereas Ingold *et al.*[23] assigned the nitric acid bands to ν_3 and ν_5 respectively, Brand and Cawthon [24] gave the reverse assignment for the bands in methyl nitrate. In the infrared spectrum of rubidium uranyl nitrate we observed no bands between 700 and 400 cm.$^{-1}$, but in this spectrum and in the spectra of uranyl nitrate di- and tri-hydrate a strong and a weak band appeared in the region 750—700 cm.$^{-1}$. These two bands are assigned to ν_3 and ν_5, but we have no criteria for distinguishing between these two vibrations and our assignment of the higher-frequency band to ν_3 is arbitrary.

In all of these spectra there are pairs of bands at *ca.* 1300 and 1500 cm.$^{-1}$ (ν_1 and ν_4 respectively) which are characteristic of the co-ordinated nitrato-group.[17] They are derived from the degenerate vibration ν_3 of the nitrate ion which is split when co-ordination changes the symmetry of the ion from D_{3h} to C_{2v}. In the spectra of uranyl nitrate di- and tri-hydrate vibrations ν_1, ν_2, ν_3, and ν_4 are split and ν_5 is very weak, whereas the out-of-plane vibration ν_6 is not split. Closely analogous splittings are found in the fluorescence spectrum of cæsium uranyl nitrate, but in the infrared spectrum of rubidium uranyl nitrate all six bands are single.

The infrared spectra are well accounted for if it is assumed that uranyl nitrate di- and tri-hydrate have structures analogous to that of rubidium uranyl nitrate [16] (I), the exact assumptions being (*a*) that each uranyl ion is surrounded by an equatorial ring of six oxygen atoms, which may or may not lie in a plane, and (*b*) that in the di- and the tri-hydrate all water molecules are directly co-ordinated with uranium. These assumptions necessarily imply that nitrato-groups are not shared between uranium atoms and it is therefore reasonable to discuss the nitrate-group vibrations in terms of the local symmetry of the molecule rather than in terms of the symmetry of the crystallographic unit-cell. The assumptions allow of only two possible structures for the molecule of the di-hydrate, (II) and (III), and two for the trihydrate, (IV) and (V).

In structures (I)—(V) the rings of six oxygen atoms are tightly packed and the planar vibrations of the nitrato-groups will be closely coupled; the in-phase and out-of-phase vibrations will have slightly different frequencies and thus each of the five planar modes will be split.

For the dihydrate, (II) alone would account for the splitting of the planar modes in the infrared spectrum. Although in structure (III) these vibrations would be split, only one of each of the pairs of vibrations would be infrared active.

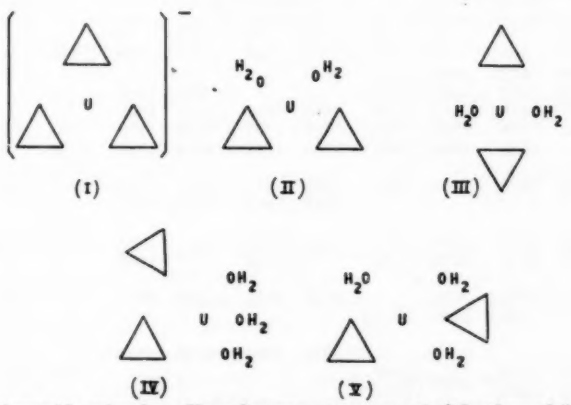
For the trihydrate, either (IV) or (V) would account for the observed splittings, but (IV) is preferred since the separation of the doublets is similar in the di- and the tri-hydrate and this implies a similar degree of coupling.

TABLE 2. *Fundamentals.*

Assignment	$RbUO_2(NO_3)_3$		$CsUO_2(NO_3)_3$ *		$UO_2(NO_3)_2,2H_2O$		$UO_2(NO_3)_2,3H_2O$	
	^{14}N	^{15}N	^{14}N	^{15}N	^{14}N	^{15}N	^{14}N	^{15}N
ν_5			708	708	706	707	720	721
	711 sh	711	713	712				
ν_3	736	736	739	738	743 sh	741 sh	743	740
			749	748	748	748	747 sh	746 sh
ν_6	803	782	805	784	801	781	800	779
B	960	960	956	956	951	951	950	951
ν_2	1023	1019	1021	1020	1026	1025	1029	1033
			1025	1024	1044	1045	1043	1046
ν_1	1276	1244	1277	split	1280	1241	1284	1246
					1311	1280	1308	1279
ν_4			1504	1471	1515	1488 sh	1517	1471
	1536	1499	1519	1480	1547	1519	1545	1515
ν_3 (H_2O)					1637	1637	1631	1634
					1650	1650	1656	1658
H_2O					3270	—	3240	—
					3360		3420	
					3560		3630	
					3690 sh		3670 sh	

* Values taken from Dieke and Duncan's fluorescence spectrum. — Not studied.

For rubidium uranyl nitrate all the planar vibrational modes should be split, but only one vibration of each pair should be infrared active. This agrees exactly with the observations.



Nitrate ions are denoted by triangles. Uranyl oxygen atoms are out of the plane of the paper, vertically above and below the uranium atoms.

Neither in the fluorescence spectrum of cæsium uranyl nitrate nor in the infrared spectra of rubidium uranyl nitrate, and uranyl nitrate di- and tri-hydrate is the out-of-plane vibration ν_6 split. This is reasonable since in vibrations of the nitrato-groups parallel to the uranyl axis there can be little interaction between neighbouring groups such as occurs in, *e.g.*, potassium nitrate.[25]

The ν_2 vibration of the water molecule is split in the spectra of uranyl nitrate di- and tri-hydrate, owing no doubt to interactions between neighbouring molecules. The bands of the water molecules in the 3000 $cm.^{-1}$ region were observed only at low dispersion and are not assigned.

Many overtones and combinations were observed in these spectra; their frequencies and probable assignments are given in Table 3. The assignments for those which showed nitrogen-isotope shifts are mostly unambiguous, but the assignments of the others are only tentative. Most of the possible combinations of two of the five planar modes of the

[25] Decius, *J. Chem. Phys.*, 1954, **22**, 1941; 1955, **23**, 1290.

nitrato-group were observed, but few involving the out-of-plane vibration. In uranyl nitrate trihydrate the two lower and the two higher frequency components of ν_2 and ν_3 both combine, but in no other case does a split fundamental yield two combination frequencies.

The infrared spectrum of uranyl nitrate hexahydrate differs considerably from the spectra discussed above: the fundamentals are given in Table 4. The hexahydrate exhibits a broad, intense band at 1366 cm.$^{-1}$, characteristic of the nitrate ion (ν_3). The nitrate ion " breathing " vibration ν_1, which is forbidden in the infrared for an isolated ion, appears here with medium intensity, presumably owing to asymmetry in the crystal environment. Similar behaviour is shown by the nitrate ion in some co-ordination compounds.[17]

The out-of-plane vibration ν_2 appears to be split into two components, separated by 32 cm.$^{-1}$, which have similar nitrogen-isotope shifts. This may be caused by association of nitrate ions in close pairs, one above the other, the two frequencies resulting from the in-phase and the out-of-phase vibration of these pairs. For an isolated pair the coupled out-of-phase vibrations would be infrared inactive, but this would not be so in the crystal if the surroundings vertically above and below each pair were different. In potassium nitrate, where nearest-neighbour nitrate ions are stacked vertically above each other in an aragonite-type lattice, this vibration is split,[25] although to a smaller extent than is that in

TABLE 3. *Overtones and combinations.*

	$RbUO_2(NO_3)_3$				$UO_2(NO_3)_2,2H_2O$				$UO_2(NO_3)_2,3H_2O$			
	^{14}N	^{14}N	^{15}N	^{15}N	^{14}N	^{14}N	^{15}N	^{15}N	^{14}N	^{14}N	^{15}N	^{15}N
Assignment	obs.	calc.	obs.	calc.	obs.	calc.	obs.	calc.	obs.	calc.	obs.	calc.
$2\nu_5$	1429	1422	1424	1422								
$2\nu_3$	1473	1472	1466	1472			1488	1486				
$2\nu_6$	1608	1606	1570	1564	1608	1602	1558	1562			1553	1558
$\nu_2 + \nu_5$	1727	1734	1733	1730	1733	1732	1733	1732	1739	1749	1739	1754
$\nu_2 + \nu_3$	1761	1759	1764	1755	1783	1787	1783	1786	1779	1772	1770	1773
$\nu_2 + \nu_3$									1795	1790	1799	1792
$A + B$	1845	1848	1845	1848	1828	1831 *	1832	1831 *	1828	1824 §	1835	1825 §
$2B$					1898	1902	1898	1902				
?									1934		1942	
$\nu_1 + \nu_5$	1990	1987	1957	1955	2008	{2017	1972	{1987	2004	2004	1969	1967
$\nu_1 + \nu_3$	2008	2009	1976	1980		{2023		{1982				
$\nu_1 + \nu_6$									2092	{2084	2024	2025
$2\nu_2$	2070	{2046	2038		2079	2088	2079	2090		{2086	2101	2092
$A + B + C$...		{2053 †	2066	2053 †								
$2B + C$									2114	2113 ‡	2119	2115 ‡
$2\nu_5 + A$					2309	2292 *	2299	2294 *				
$\nu_1 + \nu_2$	2299	2299	2268	{2263					2331	2337	2315	2312
$\nu_4 + \nu_6$	2326	2339		{2281								
?											2347	
?											2457	
?											2538	
$2\nu_1$	2545	2552	2494	2488								
$2\nu_6 + B$	2571	2566	2538	2524	2571	2553	2519	2513				
$\nu_2 + \nu_4$					2591	2591	2571	2564				
$A + B + \nu_3$...									2558	2567 §	2564	2565 §

* Assuming $A = 880$ cm.$^{-1}$. † Calc. for $CsUO_2(NO_3)_3$, using frequencies in the fluorescence spectrum. ‡ Assuming $C = 213$ cm.$^{-1}$. § Assuming $A = 874$ cm.$^{-1}$, as in the fluorescence spectrum. Figures in braces are alternative assignments.

uranyl nitrate hexahydrate. An alternative explanation would be that ν_2 is strongly coupled to a lattice vibration at 32 cm.$^{-1}$.

Only three combination frequencies and one overtone were observed in the uranyl nitrate hexahydrate spectrum: the frequencies and their probable assignments are given in Table 5.

Nitrogen-isotope Shifts.—For an isolated nitrate ion ν_1 should not shift on nitrogen-isotope substitution, since the nitrogen atom is stationary in this mode. For a co-ordinated nitrato-group there will be a small movement of the group as a whole and a small

nitrogen-isotope shift. In Dieke and Duncan's fluorescence spectrum of cæsium uranyl nitrate, shifts of 1·2 and 1·1 cm.$^{-1}$ respectively were observed in a pair of frequencies at 1020·8 and 1025·2 cm.$^{-1}$ which we assign to this mode. Such shifts would not be detected in our infrared spectra.

TABLE 4. $UO_2(NO_3)_2,6H_2O$. *Fundamentals.*

	ν_1	ν_2	ν_3	ν_4	A	A *	B	B *	$\nu_2(H_2O)$	H_2O
^{14}N	1030	803 835	1366	748	865 sh	864	941	941	1629	3270 3470 3650
^{15}N	1031	784 814	1339	747	866 sh		943		1629	—

* Values taken from Dieke and Duncan's fluorescence spectrum.
— Not studied.

TABLE 5. $UO_2(NO_3)_2,6H_2O$. *Overtones and combinations.*

	$A + B$		$\nu_2 + \nu_3$		$3\nu_2$		$2\nu_2 + B$	
	calc.	obs.	calc.	obs.	calc.	obs.	calc.	obs.
^{14}N	1806	1802	2169	2146	2505	2494	2547	2551 sh
^{15}N	1809	1799	2123	2101	2442	2451	2511	2513 sh

The nitrogen-isotope shift in the out-of-plane vibration has been discussed by Decius.[25] Since there is only one vibration of this type the shift is given directly by the Teller–Redlich rule, and the experimental values in the infrared and the fluorescence spectra of the uranyl nitrates correspond closely with the calculated values.

The two degenerate vibrations of the nitrate ion, ν_3 and ν_4, are of the same symmetry type, and the individual isotope shifts may be calculated only by assuming a particular dynamical model. No such calculation has been published, but Pryce [26] has made a calculation assuming a model having in-plane restoring forces of three types, (1) along the N–O bonds, (2) along lines joining pairs of oxygen atoms, and (3) an angle-dependent force for each O–N–O angle. This calculation predicts shifts for ν_3 and ν_4 of 29—33 cm.$^{-1}$ and 2—4 cm.$^{-1}$ respectively.

In dinitrogen pentoxide [27] and uranyl nitrate hexahydrate ν_3 is observed to shift by about 30 cm.$^{-1}$ and there is no detectable shift of ν_4. In the spectra of the uranyl nitrates having co-ordinated nitrato-groups these vibrations behave similarly; ν_1 and ν_4 each shift by 30—40 cm.$^{-1}$ and no shifts are observed for ν_3 and ν_5.

The fluorescence spectrum of cæsium uranyl nitrate follows this pattern with ν_3, ν_4, and ν_5 (assigned to Dieke and Duncan's lines *E* and *F*, *J* and *K*, and *G* and *H* respectively), but not with ν_1 (with assignment of Dieke and Duncan's lines I_3 and I_4 to $^{14}NO_3$ and I_2 and I_5 to $^{15}NO_3$) whose components have only half the expected shifts. This apparent discrepancy between the fluorescence and the infrared spectra may be due to our having used a sample of higher ^{15}N-enrichment (82 atoms % ^{15}N, compared with Dieke and Duncan's 70%): mutual interaction between the three nitrato-groups of each trinitrato-uranyl ion, when mixed isotopes are used, might reduce the apparent isotope effect.

The interpretations of the band splittings observed in these spectra, and the isotope shifts were based on original suggestions by Professor M. H. L. Pryce, F.R.S., whose help we gratefully acknowledge. We are also indebted to Dr. D. J. Millen and Dr. W. A. Runciman for valuable discussions, to Mr. T. F. Johns, for the gift of ^{15}N, and to Mr. A. M. Deane for recording the spectrum obtained with the Hilger instrument.

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HARWELL, BERKS. [*Received, June 4th*, 1958.]

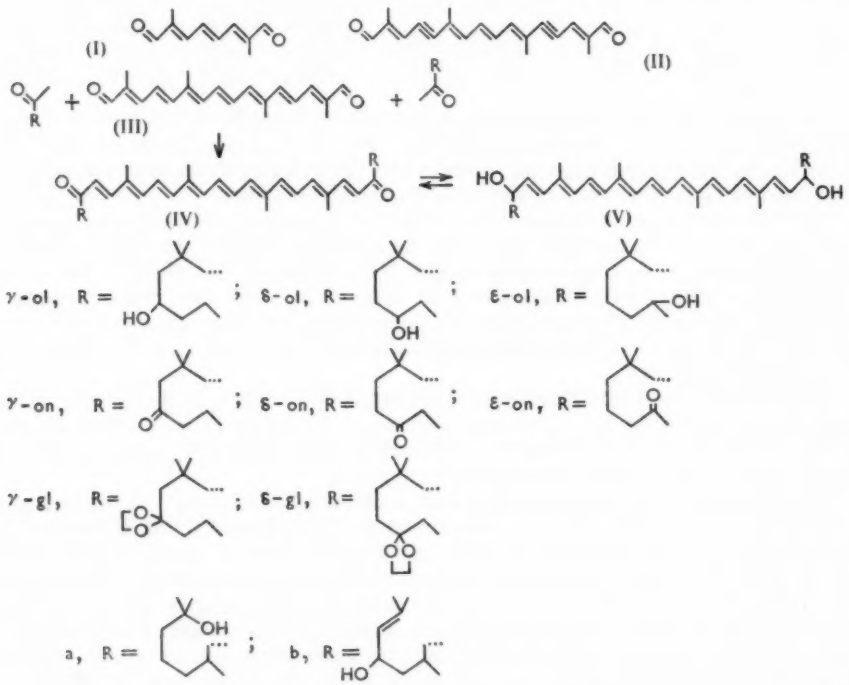
[25] M. H. L. Pryce, personal communication.
[27] Teranishi and Decius, *J. Chem. Phys.*, 1954, **22**, 896.

803. *Carotenoids and Related Compounds. Part VI.* Some Conjugated Polyene Diketones, and their Comparison with Capsorubin.*

By C. K. Warren and B. C. L. Weedon.

The formulation of capsorubin as a conjugated nona-unsaturated dione has been confirmed, and four such structures have been excluded by synthetical means.

Capsorubin, a pigment found in small amounts in red peppers (*Capsicum annuum*), contains four oxygen atoms of which two are present in hydroxyl groups. To account for the remaining oxygen atoms, the results of microhydrogenation, and the similarity in the visible spectrum with those of β-carotenone and bixin-dial, Zechmeister and Cholnoky [1] proposed for capsorubin a partial structure of type (IV). No carbonyl reactions were reported, but ketones of the type envisaged are known to be rather inert.



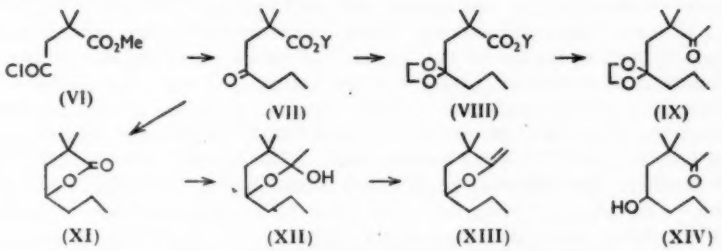
Support for the partial structure (IV) has previously been provided by the synthesis from both the C_{10} dial [2] (I) and the C_{20} dial [3] (II) of the nonaenedione (IV; R = Bu^t) which also resembled capsorubin closely in its visible-light absorption. Further confirmation of the chromophore has now been obtained in three independent ways. (i) Examination of the infrared spectrum of capsorubin revealed a band also present in the spectra of authentic compounds of the type (IV), and attributable to conjugated

* Part V, *J.*, 1954, 4168.

[1] Zechmeister and Cholnoky, *Annalen*, 1934, **509**, 269; 1935, **516**, 30; 1940, **543**, 248.
[2] Ahmad and Weedon, *J.*, 1953, 3815.
[3] *Idem*, *J.*, 1953, 3286.

carbonyl groups. (ii) Treatment of capsorubin with potassium borohydride resulted in shifts in the visible-light absorption maxima consistent with selective reduction of two terminal carbonyl groups to give a nonaene chromophore. That no further transformation had occurred was shown by regeneration of capsorubin on oxidation (see below). Similar reduction of capsanthin with potassium borohydride gave capsanthol, which has previously been prepared by the Ponndorf method.[4] (iii) Alkaline degradation of capsorubin furnished crocetin-dial (III). The reaction, which is analogous to the conversion of capsanthin into β-citraurin,[5] may be regarded as a fission of the double bonds αβ to the carbonyl groups.

The structural problem with capsorubin is therefore largely confined to the nature of the two end groups (R in IV). Zechmeister and Cholnoky [1] favoured the "γ-hydroxy-ketone structure" (IV; γ-ol), and more recently Karrer and his colleagues [6] suggested the "ε-hydroxy-ketone structure" (IV; ε-ol). In view of the scarcity of capsorubin, it seemed that these and related structures could be most readily checked by synthetical means. During our work along these lines Isler *et al.*[7] developed a route to crocetin-dial (III) which made this compound more readily available than the diacetylenic analogue (II) and greatly facilitated our investigations.



(VI) (VII) (VIII) (IX)

(XI) (XII) (XIII) (XIV)

Reaction of the half-ester acid chloride (VI) of αα-dimethylsuccinic acid with di-*n*-propylcadmium gave the keto-ester (VII; Y = Me). Hydrolysis and catalytic reduction of the resulting acid (VII; Y = H), yielded the γ-lactone (XI). This reacted with methyl-magnesium bromide to give the unsaturated ether (XIII), dehydration of the initial product (XII) occurring on distillation. With Brady's reagent the ether (XIII) readily gave a derivative of the corresponding hydroxy-ketone (XIV), but attempts to hydrolyse the ether and condense the product with aldehydes were unsuccessful, doubtless owing to the ease of cyclisation of the hydroxy-ketone (XIV). Attention was therefore directed to a related methyl ketone with a suitably protected oxygen group at position 5.

Exchange of ethylenedioxy-group [8] between the γ-keto-ester (VII; Y = Me) and 2-ethylenedioxybutane could not be achieved, presumably for steric reasons as the required reaction occurred readily with the isomeric δ-keto-ester [9] and with ethyl lævulate. However, reaction of the γ-keto-ester (VII; Y = Me) with ethylene glycol under carefully controlled conditions gave the dioxolan (VIII; Y = Me); glycol esters of the acid (VII; Y = H) formed simultaneously were converted into the starting material and re-cycled with unchanged keto-ester. Alkaline hydrolysis then gave the corresponding acid (VIII; Y = H) which on treatment with methyl-lithium furnished the required methyl ketone (IX). This formed a monosemicarbazone but, owing to hydrolysis of the protecting group, a bis-2 : 4-dinitrophenylhydrazone.

In previous condensations of polyene-dials with methyl ketones the latter were used

[4] Karrer and Hübner, *Helv. Chim. Acta*, 1936, **19**, 474; cf. Goodwin, Land, and Sissins, *Biochem. J.*, 1956, **64**, 486.
[5] Zechmeister and Cholnoky, *Annalen*, 1937, **530**, 291.
[6] Entschel, Eugster, and Karrer, *Helv. Chim. Acta*, 1956, **39**, 1263.
[7] Isler, Gutmann, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *ibid.*, 1956, **39**, 463.
[8] Dauben, Löken, and Ringold, *J. Amer. Chem. Soc.*, 1954, **76**, 1359.
[9] Warren and Weedon, following paper.

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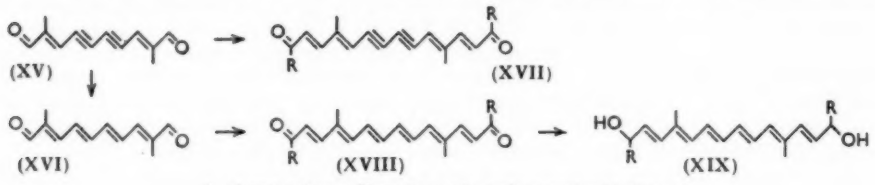
in large excess (*ca.* 500 mol.). To develop methods more suitable for use with our ketone (IX) and with related ketones, various condensations were carried out with simple methyl ketones and crocetin-dial (III) to give the nonaenediones (IV; R = Me, Pr^{i}, and Bu^{t}); also between acetone, pinacolone, and ketone (IX) with both the dienediynedial [2] (XV) and the tetraenedial (XVI) to give the derived diketones (XVII and XVIII, R = Me, and Bu^{t}; XVII, γ-gl; and XVIII, γ-gl). The tetraenedial (XVI) was obtained by partial reduction



(γ-ol and other suffixes have the values assigned above.)

of the dienediynedial (XV); the initial product gave a higher-melting form on irradiation. The spectral properties of the two isomers indicated that they were the " central di-*cis* "- and the " all-*trans* "-form respectively. Both on condensation with pinacolone gave the same product, stereomutation of the " di-*cis* "-structure occurring during the reaction.

Condensation of crocetin-dial (III) with the ketone (IX) was next studied; the yield of the dione (IV; γ-gl) ranged from 0 to 48% depending on the precise conditions used. Removal of the protecting groups by treatment with acetone and toluene-*p*-sulphonic acid gave the tetraone (IV; γ-on) in 55% yield. The isomeric tetraone (IV; δ-on) was prepared similarly (see following paper), and β-carotenone (IV; ε-on) by oxidation of β-carotene.[10] An attempt to oxidise capsorubin to a tetraketone for comparison with the three synthetic materials unfortunately failed. The possibility of converting the latter into dihydroxy-diketones, by reduction of the four carbonyl groups and subsequent selective oxidation of the two allylic hydroxyl groups, was therefore examined.

After model experiments with the hexaenes (XVIII, R = Bu^{t}; XVIII, γ-on and δ-on), the tetraketones (IV; γ-on, δ-on, and ε-on) were reduced with potassium borohydride to the corresponding tetraols (V). Selective methods for the regeneration of the polyene-diketone chromophore were studied on the hexaenediol (XIX; R = Bu^{t}). Oxidation with manganese dioxide, surprisingly, failed. Treatment with *N*-bromosuccinimide in chloroform [11] gave the hexaenedione (XVIII; R = CMe_3) in 9% yield. Oxidation with *o*-chloranil, a reagent recently developed by Braude, Linstead, *et al.*,[12] destroyed the polyene system, but substitution of *p*-chloranil for the *o*-quinone gave the hexaenedione in 20% yield. Application of the latter method to the hydroxy-compounds formed on reduction of capsanthin and capsorubin with potassium borohydride regenerated the two carotenoids. However, no nonaene diketone was obtained on treatment of the tetraol (V; γ-ol) with *p*-chloranil, and therefore the γ-hydroxy-ketone structure (IV; γ-ol) cannot represent capsorubin. Oxidation of the two isomeric tetraols (V; δ-ol and ε-ol) gave the dihydroxy-diketones (IV; δ-ol and ε-ol) in 9 and 6% overall yields from the tetraones (IV; δ-on and ε-on). These results, and those of small-scale experiments with the hexaenetetraols (XIX; γ-ol and δ-ol), suggested that hydroxyl substituents in the γ-position interfere with the oxidation of polyene glycols by *p*-chloranil, possibly owing to a cyclic attack on an intermediate carbonium ion.

Both the dihydroxy-diketones (IV; δ-ol and ε-ol) had visible-light absorption properties which resembled those of capsorubin very closely. The infrared spectra exhibited many similar characteristics but there were a number of significant differences, notably in the 1000—1100 cm.$^{-1}$ region. Further, the synthetic materials differed from the natural

[10] Kuhn and Brockmann, *Ber.*, 1932, **65**, 894; 1934, **67**, 885; *Annalen*, 1935, **516**, 123.
[11] Cf. Petracek and Zechmeister, *J. Amer. Chem. Soc.*, 1956, **78**, 1427.
[12] Braude, Linstead, and Wooldridge, *J.*, 1956, 3070.

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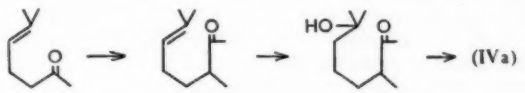
in melting point and chromatographic behaviour. There seems little doubt, in view of their mode of formation, that the synthetic compounds have an " all-*trans* "-structure. Since stereomutation of capsorubin gives no isomers with visible-light absorption at longer wavelengths,[1] the natural carotenoid must also be " all-*trans*." The differences in properties between the natural and the synthetic compounds seem greater than can be attributed to stereoisomerism involving the hydroxy-substituents [cf. similarity of the (±)- and the (−)-form of zeaxanthin [13,14]] and it is therefore concluded that capsorubin has neither of the structures (IV; δ-ol and ε-ol).

Consideration of the infrared absorption of capsorubin and synthetic nonaene diketones at 1000—1100 cm.$^{-1}$ led at one stage to the view that the natural carotenoid might possess a structure of the lycopene type. One such possibility was (IVa), but this too was excluded in the following way. A Darzens reaction between methylheptenone (XX) and ethyl α-chloropropionate yielded the ketone (XXI), which was hydrated with sulphuric acid to give the hydroxy-ketone (XXII). This on condensation with crocetin-dial (III) gave (11%) the dihydroxy-diketone (IVa), which also differed from capsorubin.



(XX) (XXI) (XXII)

The visible-light absorption properties of the polyene diketones mentioned above are summarised in Table 1. The nonaene diketones have spectra very similar to that of capsorubin, though greater fine structure is observed with the dimethyl and the di*iso*propyl diketone (IV; R = Me and Pr^{i}).

TABLE 1. *Light absorption of polyene-diketones in benzene.*

(Max. in mμ; ε × 10^{-3} in parentheses.)

Hexaenes				*Nonaenes*			
(XVIII; R = Me)	441 (67·7)	416 (68·1)		(IV; R = Me)	515 (93)	482 (104)	456 (69)
(XVIII; R = Bu^{t})	445 (75)	420 (76)	398 (47·5)	(IV; R = Pr^{i})	518 (103)	483 (115)	458 (78)
(XVIII; γ-gl)	449 (79)	424 (86)		(IV; R = Bu^{t})	518 (114)	483 (124)	
(XVIII; γ-on)	450 (84)	424 (86)		(IV; γ-gl)	518 (112)	484 (127)	
(XVIII; δ-gl) [a]	449 (78)	424 (85)		(IV; γ-on)	520 (117)	486 (123)	
(XVIII; δ-on) [a]	450 (87)	423 (89)		(IV; δ-gl) [a]	518 (116)	485 (128)	
(XVIII; δ-ol)	450 (83·5)	424 (85·5)		(IV; δ-on) [a]	520 (121)	485 (130)	
				(IV; δ-ol)	520 (123)	485 (130)	
				(IV; ε-on)	520 (113)	485 (131)	
				(IV; ε-ol)	520 (120)	485 (129)	
				(IVa)	519 (121)	485 (131)	
				Capsorubin	523 (115)	489 (132)	

Some salient features of the infrared spectra of the natural and synthetic ketones are recorded in Table 2. The conjugated carbonyl stretching frequencies of most of the synthetic ketones occur within the 1660—1672 cm.$^{-1}$ range. Both capsorubin and capsanthin exhibit a well-defined maximum in this region, the intensity of the band for capsorubin being twice that for capsanthin. Moreover there is satisfactory agreement between the intensity of the band for capsorubin and those of the synthetic nonaene diketones with large *tert.*-alkyl end groups. This provides good support for the view that capsorubin and capsanthin contain two and one conjugated carbonyl group respectively. The ε values of all these compounds are, however, considerably lower than those of the dimethyl diketones and of the *cyclo*hexenones reported in the following paper. These differences may well be due to an *s-cis*-conformation's being preferred in those acyclic polyene diketones with bulky end groups (see a discussion by Erskine and Waight [15]).

[13] Karrer and Solmssen, *Helv. Chim. Acta*, 1935, **18**, 477.
[14] Isler, Lindlar, Montavon, Rüegg, Saucy, and Zeller, *ibid.*, 1956, **39**, 2041.
[15] Erskine and Waight, Chem. Soc. Symposium on " Steric Effects in Conjugated Systems," Butterworths, 1958.

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Sterically hindered *s-trans*-conformations seem unlikely in view of the visible-light absorption characteristics. The possibility that the double bonds formed in the condensation of the polyene dialdehydes with methyl ketones have a (hindered-)*cis*-configuration also seems to be excluded by the visible spectra.

The polyene ketones all show much stronger absorption in the C=C stretching region than related polyenes, such as β-carotene, without carbonyl conjugation. The three tetraenediynediones examined exhibited a single strong band in the neighbourhood of 1587 cm.$^{-1}$. Most of the related hexaenediones had a strong band at slightly lower frequencies flanked by two bands of lower intensity. Most of the nonaenediones were characterised by two strong bands, at *ca.* 1584 and 1544 cm.$^{-1}$. The diketones possessing terminal methyl and *sec.*-alkyl groups had additional bands in the 1625—1660 cm.$^{-1}$ region.

TABLE 2. *Infrared light absorption of polyene ketones* (KBr *discs or, where indicated,* $CHCl_3$ *solutions*).

(Frequencies in cm.$^{-1}$; also ε, or an indication of relative intensity.)

	Unconjug. C=O stretching	Conjug. C=O stretching		Conjug. C=C stretching region			CH out-of-plane deformation region of conjug. *trans*-CH=CH		
Tetraenediynediones									
XVII; γ-gl		1675s			1589vs		1001m	982m	965m
XVII; γ-on	1706s	1676s			1587vs		1003m	986w	966w
XVII; δ-on*	1706s	1671s			1586vs		1001m	986s	970w
Hexaenediones									
XVIII; R = Me		1658s	1631s	1613w*	1585vs	1569w*		930s	978m
		1668 (~615)†							
XVIII; R = Bu^t		1678s		1610m	1574vs	1541m	1006s	989s	
		1677 (384)†							
XVIII; γ-gl		1675s		1607m	1562vs	1538w*	1003m	989s	970m
XVIII; γ-on	1706s	1667s		1605m	1563vs	1536m	1001w	993s	979m
XVIII; δ-gl*		1668s		1603m	1569vs	1535m	1004w	989s	
XVIII; δ-on*	1709s	1669s		1607m	1566vs	1538m	1004m	988s	
Nonaenediones									
IV; R = Me		1664s	1626s		1598s	1555s	1009s	976s*	966s
		1669 (~650)†							
IV; R = Pr^i		1675s	1658m		1585s	1545vs	1007ms	980s	970s
		1675 (~250)†	1656‡						
IV; R = Bu^t		1669s			1587s	1543vs	1004s	979s	969s
IV; γ-gl		1667s			1585s	1543vs	1007m	977s	970s
IV; γ-on	1708s	1672s			1585s	1546vs	1003ms	977s	969s
IV; δ-gl*		1672s			1584s	1546vs	1006ms	983s	968s
		1674 (387)†							
IV; δ-on*	1708s	1671s			1582s	1547vs	1004ms	980s	968s
	1715 (~660)†	1672 (~395)†							
IV; ε-on	1706s	1667s			1584s	1543vs	1003m	982s	970s
IV; ε-ol		1668s			1587s	1548vs	1007m	982m	969m
		1664 (350)†			1586s	1543vs	1004s	982s	970s
IV; δ-ol†		1664 (348)			1585s	1542vs	1003s	982s	969s
IVa†		1667m	1639s		1584s	1542vs	1005s	982s	972s
		1669 (~250)†							
Natural carotenoids									
Capsorubin†		1664 (387)			1582s	1542vs	1007s	982s	969s
Capsanthin†§		1661 (195)			1575s	1550vs	1006s	977s	966vs

* Shoulder. † In $CHCl_3$. ‡ Also 1645. § Also 1600m and 1506s. vs, very strong; s, strong; ms, medium-strong; m, medium; w, weak. * See following paper.

An outstanding feature of the spectra of "all-*trans*"-polyenes is a strong band at 964 cm.$^{-1}$ which is assigned to the CH out-of-plane deformation of the CH=CH groupings.[16,17] In all the polyene ketones now studied this band is apparently split;

[16] Lunde and Zechmeister, *J. Amer. Chem. Soc.*, 1955, **77**, 1647.
[17] *Idem, Acta Chem. Scand.*, 1954, **8**, 1421.

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thus the nonaenediones exhibit a clearly discerned triplet with maxima at *ca.* 1004, 980, and 969 cm.$^{-1}$.

On the basis of thirty-seven analyses of capsorubin and its esters, dried under considerably more vigorous conditions than are normally employed, Cholnoky *et al.*[18] have recently concluded that capsorubin contains four hydrogen atoms fewer than formerly believed. This suggests several further structures for investigation. However, the formula (IVb) proposed by the Czech workers is difficult to reconcile with the infrared spectral differences discussed above, and, as a γ-hydroxy-ketone, with the regeneration of capsorubin by chloranil oxidation of the potassium borohydride reduction product.

Experimental

M. p.s were determined on samples in evacuated sealed capillary tubes.

As far as possible, operations involving unsaturated compounds were carried out in an inert atmosphere, usually of nitrogen. Solutions of polyenes were evaporated under reduced pressure. Unless stated otherwise, alumina for chromatography was pretreated as described by Cheeseman *et al.*,[19] and was Grade III on the Brockmann and Schodder activity scale.[20] Light petroleum normally refers to the fraction of b. p. 60—80°.

Except where indicated to the contrary, visible- and ultraviolet-light absorption measurements were made on benzene solutions, and infrared absorption measurements were determined on potassium bromide discs; most of the relevant spectral data are summarised in the Tables.

Oxygen analyses were carried out by Oliver's modification [21] of Unterzaucher's method.[22]

Dimethyl αα-Dimethylsuccinate.—A mixture of ethyl cyanoacetate (298 g.), acetone (184 g.), glacial acetic acid (50 g.), benzene (250 ml.), and *p*-aminophenol (1·4 g.) was refluxed under a Dean–Stark phase-separator until 55 ml. of water had been collected (cf. Prout [23]). Distillation gave ethyl α-cyano-β-methylcrotonate (318 g., 79%), b. p. 116—120°/18 mm., m. p. 27°. Recrystallisation of a specimen from light petroleum gave the cyano-ester as needles, m. p. 33° (Vogel [24] gives m. p. 33°).

A solution of potassium cyanide (330 g.) in water (600 ml.) was added to one of the cyano-ester (317 g.) in ethanol (1·5 l.), and the mixture was kept at 20° for 40 hr. (cf. Vogel [24]). Most of the solvent was distilled off and concentrated hydrochloric acid (3 l.) was cautiously added to the residue (copious evolution of hydrogen cyanide). The mixture was refluxed for 3 hr., then cooled and extracted with ether in a continuous-extractor for 3 days. Evaporation of the extract and crystallisation of the residue from concentrated hydrochloric acid gave αα-dimethylsuccinic acid (215 g.), m. p. 141—142° (Vogel [24] gives m. p. 141°).

The acid was boiled with methanol (2·2 l.) and concentrated sulphuric acid (10 ml.) for 16 hr. Excess of solid sodium hydrogen carbonate was added and the mixture was evaporated. Isolation of the product in the usual way gave the diester (214 g.), b. p. 95—97°/21 mm., n_D^{25} 1·4212 (Bone, Sudborough, and Sprankling [25] gave b. p. 201—202°).

α-Methyl β-Hydrogen αα-Dimethylsuccinate.—A solution of dimethyl αα-dimethylsuccinate (237 g.) and potassium hydroxide (85 g.) in methanol (1·5 l.) was kept at 20° for 16 hr. The mixture was refluxed for 2 hr., then evaporated to dryness. The residue was treated with the theoretical quantity of 2N-hydrochloric acid. Isolation of the product with ether, and distillation through a fractionating column (Dufton; 20 × 2 cm.), gave an oil (160·5 g.), b. p. 104°/1·5 mm., which readily crystallised. Recrystallisation from light petroleum gave α-methyl β-hydrogen αα-dimethylsuccinate (104 g., 48%), m. p. 37—41° (Bone, Sudborough, and Sprankling [25] give m. p. 40·5—41°). The forerun from the distillation was recycled and the crude product was combined with the oil from the mother-liquors of the above crystallisation. Distillation and recrystallisation of the distillate from light petroleum, gave a further 51 g. of the half-ester, m. p. 37—41°. The total yield was 155 g. (71%).

[18] Cholnoky, Szabo, and Szabolcs, *Annalen*, 1957, **606**, 194.
[19] Cheeseman, Heilbron, Jones, and Weedon, *J.*, 1949, 3120.
[20] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.
[21] Oliver, *Analyst*, 1955, **80**, 593.
[22] Unterzaucher, *Ber.*, 1940, **73**, 391.
[23] Prout, *J. Org. Chem.*, 1953, **18**, 928.
[24] Vogel, *J.*, 1928, 2010.
[25] Bone, Sudborough, and Sprankling, *J.*, 1904, 534.

Methyl 2 : 2-*Dimethyl*-4-*oxoheptanoate* (VII; Y = Me).—A solution of the preceding half-ester (103 g.) in thionyl chloride (160 ml.) was kept for 3 days at 20°. Excess of thionyl chloride was removed under reduced pressure and the residual acid chloride in benzene (250 ml.) was slowly added to a vigorously stirred solution of di-*n*-propylcadmium (from 170 g. of *n*-propyl bromide) in benzene (1 l.). The mixture was refluxed for 1 hr., then cooled and treated with ice and 2N-sulphuric acid. The organic layer was separated, washed with saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Distillation of the residue through a fractionating column (Stedman; 30 × 2 cm.) under a partial take-off head, gave *methyl* 2 : 2-*dimethyl*-4-*oxoheptanoate* (89 g.), b. p. 118·5°/23 mm., n_D^{18} 1·4388 (Found: C, 64·0; H, 9·85. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol as yellow needles, m. p. 109—110° (Found: N, 15·15. $C_{16}H_{22}O_6N_4$ requires N, 15·3%).

2 : 2-*Dimethyl*-4-*oxoheptanoic Acid* (VII; Y = H).—A solution of the preceding keto-ester (10 g.) in 10% methanolic potassium hydroxide (75 ml.) was refluxed for 2 hr., then evaporated to dryness, and the residue was treated with an excess of 2N-hydrochloric acid. Isolation of the product with ether gave the *keto-acid* (3·8 g.) which crystallised from light petroleum as prisms, m. p. 72—73° (Found: C, 62·8; H, 9·45. $C_9H_{16}O_3$ requires C, 62·75; H, 9·35%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate as yellow prisms, m. p. 210—218° (Found: N, 15·8. $C_{15}H_{20}O_6N_4$ requires N, 15·9%).

4-*Hydroxy*-2 : 2-*dimethylheptanoic Lactone* (XI).—A solution of the preceding keto-acid (20·5 g.) in methanol (75 ml.) was shaken with Raney nickel in hydrogen at 175°/100 atm. until absorption was complete. Removal of catalyst and solvent, and distillation of the residue, gave an oil (13·5 g.), b. p. 120—125°/20 mm., and the keto-acid (3·5 g.), m. p. 70—72°. The oil, in ether, was shaken once with dilute ammonium hydrogen carbonate solution to remove traces of starting material. Isolation of the product and distillation gave the *lactone* (12·5 g.), b. p. 106—108°/15 mm., n_D^{22} 1·4355, m. p. 28—29° (unchanged on crystallisation from pentane; needles) (Found: C, 69·05; H, 10·05. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%).

Tetrahydro-3 : 3-*dimethyl*-2-*methylene*-5-*propylfuran* (XIII).—An ethereal solution (20 ml.) of methylmagnesium bromide (from 1·1 g. of magnesium) was added slowly to the preceding lactone (6·3 g.) in ether (50 ml.) at 0°. The mixture was stirred at 20° for 12 hr., boiled for 5 min., and cooled. Addition of saturated ammonium chloride and isolation of the product gave (i) the *tetrahydrofuran* (2·2 g.), b. p. 87—90°/35 mm., n_D^{21} 1·4421 (Found: C, 78·25; H, 11·95. $C_{10}H_{18}O$ requires C, 77·85; H, 11·75%), and (ii) the lactone (3·0 g.), b. p. 105—110°/17 mm., m. p. 28—29°.

Treatment of the tetrahydrofuran with Brady's reagent gave the 2 : 4-*dinitrophenylhydrazone* of 5-hydroxy-3 : 3-dimethyloctan-2-one. It crystallised from ethanol in needles, m. p. 129° (Found: N, 16·1. $C_{16}H_{24}O_5N_4$ requires N, 15·9%).

Methyl 4-*Ethylenedioxy*-2 : 2-*dimethylheptanoate* (VIII; Y = Me).—A mixture of methyl 2 : 2-dimethylheptan-4-onoate (40 g.), ethylene glycol (16·2 g.), toluene-*p*-sulphonic acid (0·1 g.), and benzene (50 ml.) was refluxed with vigorous stirring for 7 hr. under a Dean–Stark phase separator. The mixture was cooled, then washed successively with water, saturated sodium hydrogen carbonate, and water. The benzene solution was dried (Na_2SO_4) and evaporated. Distillation of the residue through a fractionating column (Stedman, 15 × 2 cm.) under a partial take-off head gave *methyl* 4-*ethylenedioxy*-2 : 2-*dimethylheptanoate* (10 g.), b. p. 144—146°/29 mm., n_D^{19} 1·4448 (Found: C, 62·3; H, 9·7. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·65%). The residue (10 g.) from the distillation consisted of a mixture of glycol esters which was converted into the original methyl ester by treatment overnight with boiling 1% (w/v) methanolic sulphuric acid (250 ml.). By combining the product with the forerun (20 g., b. p. 112—144°/29 mm.) from the preceding distillation, and recycling the material, a further quantity of the protected methyl ester was obtained. A total of three recyclisations raised the overall yield to 23·8 g. (48%) of methyl 4-ethylenedioxy-2 : 2-dimethylheptanoate.

From an attempted exchange of ethylenedioxy-group to the keto-ester from 2-ethylenedioxybutane the starting materials were recovered. A further experiment in which a small amount of ethylene glycol was added to the reaction mixture was also unsuccessful.

4-*Ethylenedioxy*-2 : 2-*dimethylheptanoic Acid* (VIII; Y = H).—Methyl 4-ethylenedioxy-2 : 2-dimethylheptanoate (8·4 g.), 5N-sodium hydroxide (7·5 ml.), and methanol (8 ml.) were refluxed together for 30 min. Water (4 ml.) was added and the mixture was refluxed for 60 min. The mixture was evaporated almost to dryness under reduced pressure; water (5 ml.)

was added and the evaporation repeated. A solution of the product in water (40 ml.) was cooled to 0° and shaken with ether (100 ml.) whilst 2N-hydrochloric acid was added until the mixture was almost neutral. Isolation of the acid product with ether yielded a gum which crystallised from pentane to give *4-ethylenedioxy-2 : 2-dimethylheptanoic acid* (6·4 g.) as prisms, m. p. 47·5—48·5° (Found: C, 61·05; H, 9·5%; equiv., 222. $C_{11}H_{20}O_4$ requires C, 61·1; H, 9·3%; equiv., 216). On admixture with 2 : 2-dimethyl-4-oxoheptanoic acid the m. p. was strongly depressed. Treatment of the protected acid with Brady's reagent gave 2 : 2-dimethyl-4-oxoheptanoic acid 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 210—218°.

5-Ethylenedioxy-3 : 3-dimethyloctan-2-one (IX).—4-Ethylenedioxy-2 : 2-dimethylheptanoic acid (11·0 g.) in ether (100 ml.) was slowly added to a vigorously stirred ethereal solution of methyl-lithium (2·35 g. in 100 ml.). The mixture was refluxed for 90 min., then cooled to 0° and treated with cold water (40 ml.). The ethereal layer was separated and the aqueous phase was extracted with ether (2 × 25 ml.). The combined ethereal solutions were washed with water, dried (Na_2SO_4–$MgSO_4$), and evaporated. Distillation of the residue gave *5-ethylenedioxy-3 : 3-dimethyloctan-2-one* (8·1 g.), b. p. 66·5—68·5°/0·6 mm., n_D^{25} 1·4502 (Found: C, 67·35; H, 10·45. $C_{12}H_{22}O_3$ requires C, 67·25; H, 10·35%). The *semicarbazone* crystallised from aqueous methanol as needles (95%), m. p. 181·5—182° (Found: C, 57·25; H, 9·2. $C_{13}H_{25}O_3N_3$ requires C, 57·55; H, 9·3%). Treatment of the ketone with Brady's reagent gave 3 : 3-*dimethyloctane-2 : 5-dione bis-2 : 4-dinitrophenylhydrazone* in 93% yield. It crystallised from aqueous dioxan as yellow needles, m. p. 178·5—179·5° (Found: C, 49·65; H, 4·95. $C_{22}H_{26}O_8N_8$ requires C, 49·8; H, 4·95%).

Ethyl 4-Ethylenedioxypentanoate.—A mixture of ethyl lævulate (30·0 g.), 2-ethylenedioxybutane (106 g.), and toluene-*p*-sulphonic acid (0·1 g.) was refluxed through a fractionating column (Stedman, 15 × 2 cm.) under a partial take-off head. At regular intervals during 12 hr., a few drops of the distillate were drawn off until a total of 27·5 ml. was collected. Solid anhydrous sodium carbonate (0·1 g.) was added and the excess of 2-ethylenedioxybutane was distilled off. Distillation of the residue from a Kon flask gave the crude product (35·0 g.), b. p. 102—115°/15 mm., n_D^{15} 1·4330. Redistillation gave ethyl γ-ethylenedioxy-*n*-valerate (26·6 g.), b. p. 107°/12 mm., n_D^{20} 1·4340 (Found: C, 57·6; H, 8·7. Calc. for $C_9H_{16}O_4$: C, 57·45; H, 8·55%). (Kuhn [26] gives b. p. 110—112°/15 mm.)

Ethyl lævulate with ethylene glycol (cf. Kuhn [26]) gave a mixture of starting materials, the required product, and the corresponding acid.

4-Ethylenedioxypentanoic Acid.—Hydrolysis of the preceding ester (24·2 g.) in methanol (26 ml.) with 5N-sodium hydroxide (26·7 ml.), and isolation of the product as described for (VIII; Y = H), gave *4-ethylenedioxypentanoic acid* which crystallised from light petroleum as prisms (17·3 g.), m. p. 35·5—37·0° (Found: C, 52·3; H, 7·7%; equiv. wt., 160. $C_7H_{12}O_4$ requires C, 52·5; H, 7·55%; equiv., 160).

5-Ethylenedioxyhexan-2-one.—Reaction of the preceding acid (7·3 g.) in ether (100 ml.) with methyl-lithium (2·3 g.) in ether (100 ml.), and isolation of the product in the usual way, gave the *ketone* (4·4 g.), b. p. 101·5—102°/12 mm., n_D^{22} 1·4411 (Found: C, 60·55; H, 9·25. $C_8H_{14}O_3$ requires C, 60·75; H, 8·9%). The *semicarbazone* (75% yield) crystallised from water as plates, m. p. 141° (Found: C, 50·6; H, 7·9. $C_9H_{17}O_3N_3$ requires C, 50·2; H, 7·95%). Treatment of the ketone with Brady's reagent gave acetonylacetone bis-2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 270° (Found: C, 46·0; H, 4·05. Calc. for $C_{18}H_{18}O_8N_8$: C, 45·6; H, 3·85%).

2 : 9-Dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (XV).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-diol (5·5 g.) in acetone (550 ml.) was shaken with manganese dioxide (110 g.; commercial, undried) for 7 hr. Isolation of the product and crystallisation from aqueous methanol gave the dial (5·2 g.), m. p. 116—117° (Ahmad and Weedon [2] give m. p. 116—117°).

Yields of only 10—52% of dial were obtained when the manganese dioxide had been dried in a vacuum over phosphoric oxide for 8 weeks.

2 : 9-Dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (XVI).—(i) A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (900 mg.) was shaken in an atmosphere of hydrogen, in the presence of Lindlar's lead-poisoned palladium catalyst (300 mg.),[27] until 2 mol. of hydrogen had been absorbed. Benzene was added to dissolve the

[26] Kuhn, *J. prakt. Chem.*, 1940, **156**, 103.
[27] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

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precipitated product, and the solution was filtered and evaporated. The residue in benzene (100 ml.) was poured on a short column of alumina. Development of the chromatogram with benzene gave a main yellow band which was eluted with the same solvent (500 ml.). A small crystal of iodine was added to the solution, and the mixture was irradiated with a 200 w lamp for 12 hr., and with diffuse daylight for 30 hr. The solution was washed with 5% aqueous sodium thiosulphate and water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from benzene–light petroleum gave the " *all*-trans "-*tetraene-dial* (470 mg.) as long orange needles, m. p. 181—182° (Found: C, 75·7; H, 7·6. $C_{12}H_{14}O_2$ requires C, 75·75; H, 7·4%), $\lambda_{max.}$ 380 and 361 mμ ($\varepsilon \times 10^{-3}$, 62·6 and 63·9 respectively), $\nu_{max.}$ 1658 (CH=O) and 9851 cm.$^{-1}$ (conjug. *trans*-CH=CH).

(ii) Partial reduction of the dienediynedial (2·18 g.) in the manner described above, removal of catalyst and solvent, and crystallisation of the residue from benzene gave a " di-*cis* "-isomer of the tetraenedial (800 mg.) as yellow needles, m. p. 176—177°, depressed to 161—164° on admixture with the " all-*trans* "-isomer. This had $\lambda_{max.}$ 380 and 361 mμ ($\varepsilon \times 10^{-3}$, 61·3 and 63·1 respectively) and $\nu_{max.}$ 1658 (C=O), 1424 and 7752 cm.$^{-1}$ (*cis*-CH=CH). Chromatography of the mother-liquors from the crystallisation afforded the " all-*trans* "-tetraenedial (314 mg.), m. p. and mixed m. p. 180—182°.

(iii) A solution of the " di-*cis* "-dial (12 mg.) in benzene (10 ml.) containing a trace of iodine, was irradiated under a 200 w lamp for 2 hr., during which the temperature of the solution rose to 50—60°. The mixture was washed with 5% sodium thiosulphate solution and water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from benzene gave the " all-*trans* "-dial (9 mg.) as long orange needles, m. p. 180—181 (mixed m. p. with an authentic sample, 180—182°; mixed m. p. with the " di-*cis* "-dial 162—165°).

Unless stated otherwise the " all-*trans* "-tetraenedial was used in subsequent reactions.

5 : 12-*Dimethylhexadeca*-3 : 5 : 11 : 13-*tetraene*-7 : 9-*diyne*-2 : 15-*dione* (XVII; R = Me).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (100 mg.) and aluminium *tert.*-butoxide (1·5 g.) in acetone (15 ml.) and benzene (15 ml.) was refluxed for 16 hr., then cooled and poured into 2N-sulphuric acid (20 ml.). The mixture was extracted with ether. The ethereal extracts were washed with saturated sodium hydrogen carbonate and water, dried, (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina gave a main yellow band which was eluted. Evaporation of the solution, and crystallisation of the residue from benzene–light petroleum, gave the dione (40 mg.) as yellow prisms, m. p. 149—151° (Ahmad and Weedon [3] give m. p. 149—151°).

2 : 2 : 6 : 13 : 17 : 17 - *Hexamethyloctadeca*-4 : 6 : 12 : 14 - *tetraene* - 8 : 10 - *diyne* - 3 : 16 - *dione* (XVII; R = Bu^t).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (100 mg.) and aluminium *tert.*-butoxide (1·5 g.) in pinacolone (1·0 ml.) and benzene (15 ml.) was refluxed for 16 hr., then cooled and poured into 2N-sulphuric acid. Isolation of the product as in the preceding experiment gave the *dione* which crystallised from benzene–light petroleum in yellow needles (70 mg.), m. p. 153—155° (Found: C, 81·6; H, 8·7. $C_{24}H_{36}O_2$ requires C, 82·25; H, 8·65%), $\lambda_{max.}$ in ethanol, 402, 372, 345, and 255 mμ ($\varepsilon \times 10^{-3}$, 42·3, 44·2, 35·2, and 14·4 respectively).

4 : 23 - *Di*(*ethylenedioxy*) - 6 : 6 : 10 : 17 : 21 : 21 - *hexamethylhexacosa* - 8 : 10 : 16 : 18 - *tetraene* - 12 : 14-*diyne*-7 : 20-*dione* (XVII; γ-gl).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (200 mg.) and aluminium *tert.*-butoxide (2·0 g.) in 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (2·5 ml.) and benzene (10 ml.) was refluxed for 20 hr., then cooled and poured into 0·5N-sulphuric acid (100 ml.). The mixture was extracted with ether. The ethereal extracts were washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. The excess of ethylenedioxydimethyloctanone was distilled off at 60° (bath temp.)/10^{-6} mm. Chromatography of the residue in benzene (25 ml.) on alumina and isolation of the main yellow band yielded a solid (140 mg.). Crystallisation from benzene–light petroleum gave the *dione* (109 mg.) as yellow needles, m. p. 104—105° (Found: C, 74·95; H, 8·85. $C_{36}H_{50}O_6$ requires C, 74·7; H, 8·7%), $\lambda_{max.}$ in *n*-hexane 401, 371, 346, and 254 mμ ($\varepsilon \times 10^{-3}$, 45·2, 50·0, 42·1, and 18·3 respectively).

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 16 : 18-*tetraene*-12 : 14-*diyne*-4 : 7 : 20 : 23-*tetraone* (XVII; γ-on).—A solution of the preceding dione (95 mg.) in acetone (25 ml.) containing toluene-*p*-sulphonic acid (20 mg.) was refluxed for 2 hr. The mixture was cooled, diluted with ether (100 ml.), washed with saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina,

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isolation of the main yellow band, evaporation, and crystallisation of the residue from benzene–light petroleum gave the tetraone (26 mg.) as yellow prisms, m. p. 94—95°, $\lambda_{max.}$ in *n*-hexane 402, 372, 346, and 254 mμ ($\varepsilon \times 10^{-3}$, 42·4, 46·8, 39·7, and 17·2 respectively).

5 : 12-*Dimethylhexadeca*-3 : 5 : 7 : 9 : 11 : 13-*hexaene*-2 : 15-*dione* (XVIII; R = Me).—5% Ethanolic potassium hydroxide (2 ml.) was added to 2 : 9-dimethyl-2 : 4 : 6 : 8-tetraene-1 : 10-dial (78 mg.) in acetone (7·0 ml.), and the solution was kept for 20° for 30 min. Benzene (100 ml.) was added, and the solution was washed with 2N-sulphuric acid, saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue in benzene on alumina, isolation of the main yellow band, evaporation, and crystallisation of the residue from benzene–light petroleum gave the ***dione*** (38 mg.) as orange plates, m. p. 171—172° (Found: O, 12·0. $C_{18}H_{22}O_2$ requires O, 11·85%).

2 : 2 : 6 : 13 : 17 : 17-*Hexamethyloctadeca*-4 : 6 : 8 : 10 : 12 : 14-*hexaene*-3 : 16-*dione* (XVIII; R = Bu^t).—(i) A solution of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (128 mg.) and aluminium *tert.*-butoxide (1·0 g.) in pinacolone (2 ml.) and benzene (10 ml.) was refluxed for 16 hr., then cooled and poured into 2N-sulphuric acid (20 ml.). Extraction with benzene and isolation of the product as in the preceding experiment gave the ***dione*** which crystallised from benzene–light petroleum in yellow needles (153 mg.), m. p. 206—207° (Found: C, 81·5; H, 9·6. $C_{24}H_{34}O_2$ requires C, 81·3; H, 9·65%). Condensation of the "di-*cis*"-tetraenedial with pinacolone gave the same product.

Potassium borohydride (150 mg.) was added during 1 hr. to a boiling solution of the dione (196 mg.) in methanol (10 ml.). The solution was cooled, and 0·05N-sulphuric acid (40 ml.) was added. Isolation of the product with ether and crystallisation from aqueous ethanol gave the diol (173 mg.) as an unstable, microcrystalline, yellow solid, m. p. 152—156°, $\lambda_{max.}$ 399 and 376 mμ ($\varepsilon \times 10^{-3}$, 65·7 and 63·4 respectively), $\nu_{max.}$ 3390 $cm.^{-1}$ (no absorption in the carbonyl region).

(ii) A solution of the preceding diol (10 mg.) and chloranil (15 mg.) in benzene (1·5 ml.) was kept at 20° for 18 hr., then poured on a column of alumina, and the chromatogram was developed with benzene. The main yellow band yielded the hexaenedione (2 mg.), m. p. 202—204°, mixed m. p. with a sample from (i), 202—205°, $\lambda_{max.}$ 445 and 420 mμ.

Oxidation of the diol (10 mg.) in benzene (1·5 ml.) with tetrachloro-*o*-benzoquinone (15 mg.) (cf. Braude, Linstead, and Wooldridge [12]) at 80° for 30 min., or 20° for 16 hr., gave none of the required dione. Treatment of the diol (8 mg.) in acetone (1 ml.) with manganese dioxide (240 mg.) at 20° for 65 hr., and finally under reflux for 3·5 hr., yielded no dione; the diol (2 mg.; estimated spectroscopically) was recovered.

(iii) A solution of *N*-bromosuccinimide (14 mg.) in chloroform (10 ml.; free from ethanol and hydrochloric acid) was added to the diol (14 mg.) in the same solvent (10 ml.). One minute later, powdered *N*-phenylmorpholine (14 mg.) was added with stirring. After being refluxed for 30 min., the mixture was cooled and washed with 2N-hydrochloric acid, aqueous sodium hydrogen carbonate, and water. The chloroform solution was dried (Na_2SO_4) and evaporated. Chromatography of the residue from benzene on alumina, isolation of the main yellow band, evaporation, and crystallisation of the residue from light petroleum gave the hexaenedione (1·2 mg.) as yellow needles, m. p. and mixed m. p. 206—207°, $\lambda_{max.}$ 445 and 420 mμ.

4 : 23-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 17 : 21 : 21-*hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-7 : 20-*dione* (XVIII; γ-gl).—A solution of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (200 mg.), aluminium *tert.*-butoxide (1·0 g.), and 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (2·0 g.) in benzene (10 ml.) was refluxed for 20 hr., then cooled and diluted with benzene (100 ml.). The solution was washed with 0·05N-sulphuric acid, then with saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. The excess of ethylenedioxydimethyloctanone was distilled off at 60° (bath temp.)/10^{-6} mm. Chromatography of the residue in benzene (25 ml.) on alumina, isolation of the main yellow band, evaporation, and crystallisation of the residue from benzene–light petroleum gave the dione (56 mg.) as yellow needles, m. p. 124—126·5°.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-4 : 7 : 20 : 23-*tetraone* (XVIII; γ-on).—(i) A solution of the preceding dione (40 mg.) and toluene-*p*-sulphonic acid (10 mg.) in acetone (25 ml.) was refluxed for 90 min., then cooled and diluted with benzene (50 ml.). The solution was washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Isolation of the product by chromatography from

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benzene on alumina and crystallisation from benzene–light petroleum gave the *tetraone* (16 mg.) as yellow needles, m. p. 119—124° (Found: C, 77·6; H, 9·55. $C_{32}H_{46}O_4$ requires C, 77·7; H, 9·35%).

(ii) Condensation of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (152 mg.) with 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (2·0 g.), in the manner described above, and hydrolysis of the crude product, gave the tetraone (35 mg.), m. p. 119—124°.

(iii) A solution of 6 : 6 : 10 : 17 : 21 : 21-hexamethylhexacosa-8 : 10 : 16 : 18-tetraene-12 : 14-diyne-4 : 7 : 20 : 23-tetraone (25 mg.) in ethyl acetate (4 ml.) was shaken in hydrogen in the presence of Lindlar's catalyst [27] until 2 mol. of hydrogen had been absorbed. The catalyst and solvent were removed and the residue in benzene (*ca.* 10 ml.), containing a trace of iodine, was exposed to diffuse daylight for 8 hr. The solution was washed with 5% aqueous sodium thiosulphate, dried, and evaporated. Chromatography of the residue from benzene on alumina furnished the hexaenetetraone (2 mg.), m. p. and mixed m. p. 119—123°, $\lambda_{max.}$ 449 and 424 mμ.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-4 : 7 : 20 : 23-*tetraol* (XIX; γ-ol).—Potassium borohydride (20 mg.) was added during 15 min. to a boiling solution of the preceding tetraone (23 mg.) in methanol (15 ml.). 2N-Sodium hydroxide (1·0 ml.) was added, and the solution was refluxed for 15 min., cooled, diluted with ether (50 ml.), washed with water, dried (Na_2SO_4), and evaporated. The residual unstable oil exhibited visible light absorption maxima at 400 and 377 mμ, and (in CCl_4) an infrared absorption maximum at 3360 cm.$^{-1}$, but no absorption in the carbonyl region. The tetraol content was estimated spectrally as 5 mg. Oxidation with chloranil (15 mg.) in benzene (1 ml.) at 20° for 16 hr., and chromatography, gave no product with a hexaenedione chromophore.

Reduction of the tetraone, and treatment of the crude reaction mixture with 0·05N-sulphuric acid, gave a product with $\lambda_{max.}$ 400 and 377 mμ, but no infrared absorption maximum in the hydroxyl or carbonyl region; presumably cyclisation of the initial product had occurred to give a bistetrahydrofuran derivative.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-3 : 7 : 20 : 24-*tetraol* (XIX; δ-ol) *and the* 3 : 24-*Dihydroxy*-7 : 20-*dione* (XVIII; δ-ol).—Potassium borohydride (50 mg.) was added during 15 min. to a boiling solution of 6 : 6 : 10 : 17 : 21 : 21-hexamethylhexacosa-8 : 10 : 12 : 14 : 16 : 18-hexaene-3 : 7 : 20 : 24-tetraone [9] (40 mg.) in methanol (5 ml.). 2N-Sodium hydroxide (1·0 ml.) was then added, and the solution was refluxed for 15 min., cooled, and diluted with water (20 ml.). The product was isolated with ether and crystallised from benzene–light petroleum to give the tetraol (9·4 mg.) as an unstable, microcrystalline yellow solid, m. p. 110—120°, $\lambda_{max.}$ 399 and 376 mμ ($\varepsilon \times 10^{-3}$, 64·7 and 66·5 respectively), $\nu_{max.}$ 3370 cm.$^{-1}$ (no absorption in the carbonyl region).

A solution of the tetraol (6·5 mg.) and chloranil (7·5 mg.) in benzene (2 ml.) was kept at 20° for 65 hr., then poured on a column of alumina. The chromatogram was developed with benzene–chloroform (2 : 1). Isolation of the main band, and crystallisation from benzene–light petroleum, gave the hydroxy-dione (0·7 mg.) as orange-yellow prisms, m. p. 107—110°.

5 : 9 : 14 : 18-*Tetramethyldocosa*-3 : 5 : 7 : 9 : 11 : 13 : 15 : 17 : 19-*nonaene*-2 : 21-*dione* (IV; R = Me).—A mixture of crocetin-dial (106 mg.), acetone (7 ml.), and 5% ethanolic potassium hydroxide (2 ml.) was shaken at frequent intervals and kept at 20° for 45 min. Benzene (60 ml.) was added and the mixture was washed with water, 2N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water. The solution was dried (Na_2SO_4) and evaporated. Chromatography of the residue in benzene on alumina, and crystallisation from benzene–light petroleum, gave the dione (70 mg.) as deep-red plates, m. p. 179—181° (Found: O, 8·8. $C_{26}H_{32}O_2$ requires O, 8·5%).

2 : 6 : 10 : 15 : 19 : 23-*Hexamethyltetracosa*-4 : 6 : 8 : 10 : 12 : 14 : 16 : 18 : 20-*nonaene*-3 : 22-*dione* (IV; R = Pr^i).—A mixture of crocetin-dial (49 mg.), 3-methylbutan-2-one (4 ml.) and 5% ethanolic potassium hydroxide was shaken occasionally and kept at 20° for 24 hr. Isolation of the crude product, as in the previous experiment, and crystallisation from benzene–light petroleum gave the *dione* (46·5 mg.) as purple plates, m. p. 187° (Found: O, 7·6. $C_{30}H_{40}O_2$ requires O, 7·4%).

2 : 2 : 6 : 10 : 15 : 19 : 23 : 23-*Octamethyltetracosa*-4 : 6 : 8 : 10 : 12 : 14 : 16 : 18 : 20-*nonaene*-3 : 22-*dione* (IV; R = Bu^t).—(i) A mixture of crocetin-dial (30 mg.), pinacolone (2 ml.), aluminium *tert.*-butoxide, and benzene (10 ml.) was refluxed for 16 hr., then cooled, diluted with benzene (50 ml.), and washed with 2N-sulphuric acid, saturated sodium hydrogen carbonate

solution, and water. The benzene solution was dried (Na_2SO_4) and evaporated. Crystallisation of the residue from benzene–light petroleum gave the *dione* (11 mg.) as purple plates, m. p. 221—222° (Found: C, 82·75; H, 9·45. $C_{32}H_{44}O_2$ requires C, 83·4; H, 9·65%). Ahmad and Weedon [2] give m. p. 220—221° (Kofler block). Chromatography of the mother-liquors on alumina gave a main red band which was eluted with benzene. Evaporation of the resultant solution, and crystallisation of the residue from benzene–light petroleum, gave a further 11 mg. of the dione (total yield 22 mg., 49%).

(ii) A mixture of crocetin-dial (44 mg.), pinacolone (3 ml.), and 5% methanolic potassium hydroxide (3 ml.) was warmed to effect complete dissolution of the dial, and was then kept at 20° for 20 hr. After addition of $2\frac{1}{2}$% methanolic potassium hydroxide (15 ml.), the solution was kept at 20° for a further 50 hr. The crystalline precipitate was filtered off and recrystallised from benzene–light petroleum, to give the dione (10 mg.), m. p. and mixed m. p. 221—222°. After being diluted with chloroform (50 ml.), the filtrate from the reaction mixture was washed successively with water, 2N-sulphuric acid, saturated aqueous sodium hydrogen carbonate, and water. The chloroform solution was dried (Na_2SO_4) and evaporated. Chromatography of the residue from benzene on alumina gave a further 5 mg. of the dione (total yield 15 mg., 23%).

4 : 29-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 14 : 19 : 23 : 27 : 27-*octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-7 : 26-*dione* (IV; γ-gl).—A mixture of crocetindial (240 mg.), 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (7·0 g.), and 5% ethanolic potassium hydroxide (9·0 ml.) was refluxed for 30 min., then cooled rapidly, diluted with benzene (100 ml.), and washed successively with water, 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water. The benzene solution was dried (Na_2SO_4) and evaporated. The oily residue was diluted with light petroleum (50 ml.). When kept overnight at 0°, the solution deposited deep-red leaflets (265 mg., 48%), m. p. 178—180°. Recrystallisation from benzene–light petroleum gave the *dione* as deep red leaflets, m. p. 182—183° (Found: C, 77·05; H, 9·55. $C_{44}H_{64}O_6$ requires C, 76·7; H, 9·35%).

Evaporation of the crude reaction product at 60°/10^{-6} mm., and chromatography of the residue, gave the dione in 22% yield. Longer reaction resulted in destruction of the dione.

Attempts to condense crocetin-dial with the methyl ketone by means of 5% methanolic potassium hydroxide at 20°, boiling 5% potassium hydroxide in ethyl cellosolve, or aluminium *tert.*-butoxide in boiling benzene gave none of the required product.

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *Octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-4 : 7 : 26 : 29-*tetraone* (IV; γ-on).—A solution of the preceding nonaenedione (260 mg.) and toluene-*p*-sulphonic acid (25 mg.) in acetone (50 ml.) was refluxed for 1 hr., cooled, diluted with benzene (150 ml.), and washed with saturated aqueous sodium hydrogen carbonate and water. The benzene solution was dried (Na_2SO_4) and evaporated. Crystallisation of the residue from benzene–light petroleum gave the *tetraone* (123 mg.) as purple leaflets, m. p. 159° (Found: C, 80·35; H, 9·9. $C_{40}H_{56}O_4$ requires C, 79·95; H, 9·4%).

Chromatography of the crude product did not raise the yield.

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *Octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-4 : 7 : 26 : 29-*tetraol* (V; γ-ol).—Potassium borohydride (100 mg.) was added during 30 min. to a boiling solution of the preceding tetraone (98 mg.) in methanol (15 ml.). 2N-Sodium hydroxide (2 ml.) was added, and the solution was refluxed for 15 min. and then cooled. Benzene (100 ml.) was added and the solution was washed with water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from benzene–light petroleum gave the tetraol (15·5 mg.) as an unstable, microcrystalline, red solid, m. p. 174—180° (sintered at 155°), $\lambda_{max.}$ 480, 450, and 426 mμ (ε × 10^{-3}, 93, 105, and 81 respectively), $\nu_{max.}$ 3380 $cm.^{-1}$ (no absorption in the carbonyl region).

Oxidation of the tetraol (14 mg.) with chloranil (13 mg.) in benzene–ethanol (9 : 1; 5 ml.) at 20° for 16 hr. gave no product with a nonaenedione chromophore. Another experiment was followed spectroscopically for 8 days, but gave no indication of nonaenedione formation. Oxidation of the tetraol in chloroform with *N*-bromosuccinimide, or in acetone with manganese dioxide, also gave no nonaenedione.

3 : 30 - *Dihydroxy* - 6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *octamethyltriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-7 : 26 - *dione* (IV; δ-ol).—Potassium borohydride (60 mg.) was added during 10 min. to a boiling solution of 6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - octamethyldotriaconta - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - nonaene-3 : 7 : 26 : 30-tetraone [9] (50 mg.) in

methanol (10 ml.). Isolation of the crude product as in the previous experiment, chromatography from benzene on alumina, and elution of the main yellow band with 1% ethanol in benzene, gave a solution of the nonaene tetraol (38 mg., estimated spectroscopically), $\lambda_{max.}$ 476, 446, and 422 mμ. Evaporation gave a yellow oil which was dissolved in benzene–ethanol (19 : 1; 30 ml.). Chloranil (42 mg.) was added, and the solution kept at 20° and examined spectrographically at intervals. After 22 hr. the reaction had ceased. Addition of further chloranil (10, 10, 10, and 80 mg.) periodically produced only a small increase in the proportion of the required chromophore. After 144 hr. the reaction mixture was evaporated. Chromatography of the residue from benzene on alumina, elution of the main red band with 1—2% of ethanol in benzene, and crystallisation from benzene–light petroleum gave the *dihydroxy-dione* (4·5 mg.) as purple leaflets, m. p. 170—171° (Found: O, 10·6. $C_{40}H_{60}O_4$ requires O, 10·6%), $\nu_{max.}$ 3620, 3400, and 1664 cm.$^{-1}$. In a mixed chromatogram on alumina the dihydroxy-dione was less strongly adsorbed than capsorubin.

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *Octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-2 : 7 : 26 : 31-*tetraol* (V; ε-ol) *and the* 2 : 31-*Dihydroxy*-7 : 26-*dione* (IV; ε-ol).—Oxidation of β-carotene by the method of Kuhn and Brockmann [10] gave β-carotenone as purple leaflets, m. p. 171—172° [Kuhn *et al.*[10] give m. p. 174—175° (corr.)].

Reduction of β-carotenone (39 mg.) in boiling methanol (7 ml.) with potassium borohydride (42 mg.), and purification of the product as in the preparation of the isomeric 4 : 7 : 26 : 29-tetraol, gave the 2 : 7 : 26 : 31-tetraol (19 mg.) as an unstable, microcrystalline red solid, m. p. 180—185° (sintered at 160°), $\lambda_{max.}$ 480, 450, and 425 mμ (ε × 10^{-3}, 103, 106, and 73·5 respectively) $\nu_{max.}$ 3380 cm.$^{-1}$.

A solution of the tetraol (40 mg.) and chloranil (36 mg.) in benzene (9 ml.) and ethanol (1 ml.) was kept at 20° for 20 hr. and then evaporated. Chromatography of the residue from benzene–chloroform on alumina, isolation of the main band, and crystallisation from benzene–light petroleum gave the *dihydroxy-dione* (8 mg.) as purple prisms, m. p. 166° (Found: C, 79·05; H, 10·85. $C_{40}H_{60}O_4$ requires C, 79·4; H, 10·0%). In a mixed chromatogram on alumina with 0·5% ethanol in benzene as the eluent, the dihydroxy-dione was less strongly adsorbed than capsorubin.

Reduction and Regeneration of Capsanthin.—Capsanthin was isolated from *Capsicum annuum* as red needles, m. p. 181—182°, $\lambda_{max.}$ 483 mμ, inflexion 518 mμ (ε × 10^{-3}, 121 and 95 respectively).

Potassium borohydride (40 mg.) was added during 45 min. to a boiling solution of capsanthin (30·5 mg.) in methanol (10 ml.). 2N-Sodium hydroxide (1·0 ml.) was then added and the mixture was refluxed for 15 min. Isolation of the crude product in the usual way, and crystallisation from benzene–light petroleum, gave capsanthol (14 mg.) as dark red prisms, m. p. 180—182°, depressed to 170—176° on admixture with capsanthin. It had absorption maxima at 483 and 455 mμ (ε × 10^{-3}, 90 and 95 respectively), and at 3370 cm.$^{-1}$. (For the product of Ponndorf reduction, Karrer and Hubner [4] give m. p. 175—176°, $\lambda_{max.}$ 492 and 462 mμ.)

A solution of capsanthol (7·5 mg.) and chloranil (8 mg.) in benzene–ethanol (19 : 1; 5 ml.) was kept at 20° for 22 hr., then evaporated. Chromatography of the residue on alumina, elution of the main red band with 1% of ethanol in benzene, evaporation, and crystallisation from benzene–light petroleum gave capsanthin (2 mg.) as red needles, m. p. and mixed m. p. 181°. The visible and infrared spectra were identical with those of natural capsanthin. No separation was observed in a mixed chromatogram.

Reduction and Regeneration of Capsorubin.—Potassium borohydride (11 mg.) was added during 100 min. to a boiling solution of capsorubin (1·1 mg.) in methanol (3 ml.). 2N-Sodium hydroxide (0·5 ml.) was added and the mixture was refluxed for 10 min. Isolation of the product in the usual way and chromatography from benzene on alumina gave a yellow band which was eluted with 1% of ethanol in benzene. The resulting solution of the tetraol (40% spectroscopic yield) had $\lambda_{max.}$ 476 and 447 mμ.

The solution of the tetraol was evaporated and the residue was dissolved in benzene–ethanol (19 : 1; 2 ml.). Chloranil (0·5 mg.) was added and the solution kept at 20° for 92 hr. (a further 0·1 mg. of chloranil was added after 13 hr.). The course of the reaction was followed spectroscopically, and a smooth regeneration of the capsorubin spectrum was observed. Evaporation of the reaction mixture, and chromatography of the residue from benzene on alumina, gave a main red band which was eluted with 1·5% of ethanol in benzene. Its visible-light absorption spectrum was identical with that of capsorubin, and no separation was observed in a mixed chromatogram with the natural carotenoid.

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Alkaline Fission of Capsorubin.—(i) A solution of capsorubin (0·6 mg.) in benzene (0·5 ml.) and 10% ethanolic potassium hydroxide (2 ml.) was refluxed for 2 hr. The mixture was cooled, diluted with benzene (20 ml.), washed with water, 0·5N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina gave three bands: A (most strongly adsorbed), $\lambda_{max.}$ 521 and 489 mμ (cf. capsorubin, $\lambda_{max.}$ 523 and 489); B, $\lambda_{max.}$ 499 and 469 mμ; and C, $\lambda_{max.}$ 474 and 446 mμ (cf. crocetin-dial, $\lambda_{max.}$ 474 and 446 mμ). Band C (spectroscopic yield 0·06 mg., 20%) did not separate from crocetin-dial in a mixed chromatogram.

(ii) Hydrolysis of capsorubin (17 mg.) in the above manner, evaporation of band C, and crystallisation of the residue from benzene–light petroleum, gave crocetin-dial (0·2 mg.) as needles, m. p. 189° (undepressed on admixture with an authentic specimen, m. p. 190°), $\lambda_{max.}$ 474 and 446 mμ.

3 : 7-*Dimethyloct-6-en-2-one* (XXI).—Powdered sodium methoxide (80 g.) was added during 40 min. to a stirred and cooled (ice–salt) mixture of ethyl α-chloropropionate (14·3 g.) and 6-methylhept-5-en-2-one (111 g.). The mixture was stirred at 20° for 4 hr., then again cooled (ice) and 15% methanolic potassium hydroxide (550 ml.) was added. The mixture was stirred at 20° for 2 hr., then diluted with water (1 l.) and extracted with ether. The aqueous layer was acidified with concentrated hydrochloric acid and extracted with ether. The ethereal extract was dried ($MgSO_4$) and evaporated. The residue was heated at 140° for 1½ hr., cooled, and dissolved in benzene–ether (1 : 1). The solution was washed with 2N-sodium carbonate and water, dried ($MgSO_4$), and evaporated. Distillation of the residue gave 3 : 7-*dimethyloct-6-en-2-one* (24·8 g.), b. p. 192—197°, 88—90°/14 mm., n_D^{20} 1·4434 (Found: C, 77·5; H, 11·95. $C_{10}H_{18}O$ requires C, 77·85; H, 11·75%), $\nu_{max.}$ (liquid film) 1706 cm.$^{-1}$. The *semicarbazone* (80% yield) crystallised from aqueous ethanol in prisms, m. p. 61—64° (Found: C, 62·65; H, 10·0. $C_{11}H_{21}ON_3$ requires C, 62·5; H, 10·0%).

7-*Hydroxy*-3 : 7-*dimethyloctan*-2-*one* (XXII).—3 : 7-Dimethyloct-6-en-2-one (10·0 g.) was shaken with 35% (w/v) sulphuric acid (200 ml.) for 5½ hr. The mixture was extracted with ether, cooled at −40°, and stirred vigorously whilst 40% aqueous sodium hydroxide was added cautiously until the mixture was alkaline. The mixture was warmed to 20°, sufficient water was added to dissolve the inorganic salts, and the solution was extracted continuously with ether for 16 hr. The extract was dried ($MgSO_4$) and evaporated, and the residue was distilled to give the *hydroxy-ketone* (2·9 g.), b. p. 64°/0·1 mm., n_D^{26} 1·4444 (Found: C, 69·8; H, 11·8. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7%), $\nu_{max.}$ (liquid film) 3360 and 1705 cm.$^{-1}$.

Similar treatment of 6-methylhept-5-en-2-one (10·0 g.) gave 6-hydroxy-6-methylheptan-2-one (6·3 g.), b. p. 72°/0·2 mm., n_D^{20} 1·4445 (Found: C, 66·4; H, 11·3. Calc. for $C_8H_{16}O_2$: C, 66·6; H, 11·2%) (Rupe and Schlochoff [18] give b. p. 106°/9 mm.), $\nu_{max.}$ (liquid film) 3360 and 1708 cm.$^{-1}$.

2 : 31-*Dihydroxy*-2 : 6 : 10 : 14 : 19 : 23 : 27 : 31-*octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-7 : 26-*dione* (IVa).—A mixture of crocetin-dial (64 mg.), 7-hydroxy-3 : 7-dimethyloctan-2-one (0·9 g.) and 5% ethanolic potassium hydroxide (3 ml.) was shaken occasionally and kept at 20° for 3½ hr., then refluxed for 30 min., cooled, and diluted with benzene (50 ml.), washed with water, 0·05N-sulphuric acid, saturated aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated, finally at 60° (bath temp.)/10^{-6} mm. The residue in benzene–chloroform (17 : 3; 50 ml.) was poured on a column of alumina, and the chromatogram was developed with 1% of ethanol in benzene. Isolation of the main red band, evaporation, and crystallisation from benzene–light petroleum gave the *dihydroxy-dione* (12·5 mg.), m. p. 133—134° (Found: O, 10·4. $C_{40}H_{60}O_4$ requires O, 10·6%), $\nu_{max.}$ 3530, 3390, 1667, and 1639 cm.$^{-1}$. A further 2 mg. of product were obtained by chromatography of the mother-liquors. In a mixed chromatogram on alumina the dihydroxy-dione was less strongly adsorbed than capsorubin.

The authors are greatly indebted to Dr. O. Isler for a generous gift of crocetin-dial, and Professor L. Zechmeister for one of capsorubin. They thank Dr. Rashid Ahmad and Mr. M. S. Barber for their assistance with some of the experiments, and Dr. E. S. Waight for helpful discussions on the spectral data. One of the authors (C. K. W.) is indebted to the Distillers Co. Ltd. for a research bursary. Analyses were carried out in the microanalytical (Miss J.

[18] Rupe and Schlochoff, *Ber.*, 1905, **38**, 1503.

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Cuckney) laboratory of this Department, and the infrared (Mr. R. L. Erskine) and some of the ultraviolet and visible (Mrs. A. I. Boston) light absorption measurements in the spectrographic laboratory.

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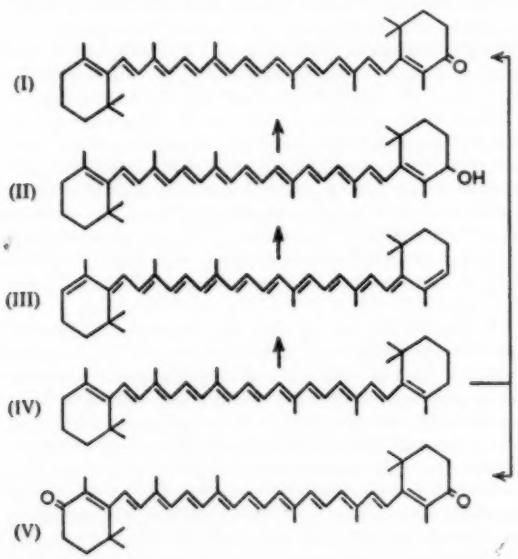
804. *Carotenoids and Related Compounds. Part VII.* Synthesis of Canthaxanthin and Echinenone.*

By C. K. WARREN and B. C. L. WEEDON.

A method has been developed for the introduction of the 2 : 6 : 6-trimethyl-3-oxo*cyclo*hex-1-enyl group into polyenes, and used to synthesise canthaxanthin and echinenone from crocetin-dial and β-*apo*-2-carotenal respectively.

ECHINENONE was first isolated from the gonads of the sea urchin *Paracentrotus* (*Strongylocentrotus*) *lividus* by Lederer who suggested that it was a keto-derivative of β-carotene.[1] Goodwin and Taha [2] later formulated echinenone as 4-oxo-β-carotene (I), and advanced arguments for its identity with both myxoxanthin [3] and aphanin [4] from the blue algæ *Oscillatoria rubescens* and *Aphanizomenon flos-aquae* respectively.



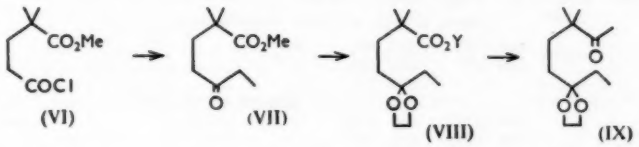
By hydrolysis of the boron trifluoride complex of dehydro-β-carotene (III) Wallcave and Zechmeister [5] obtained "*iso*cryptoxanthin" for which they deduced the structure (II). Oppenauer oxidation of this compound by Ganguly, Krinsky, and Pinckard [6] gave

* Part VI, preceding paper.

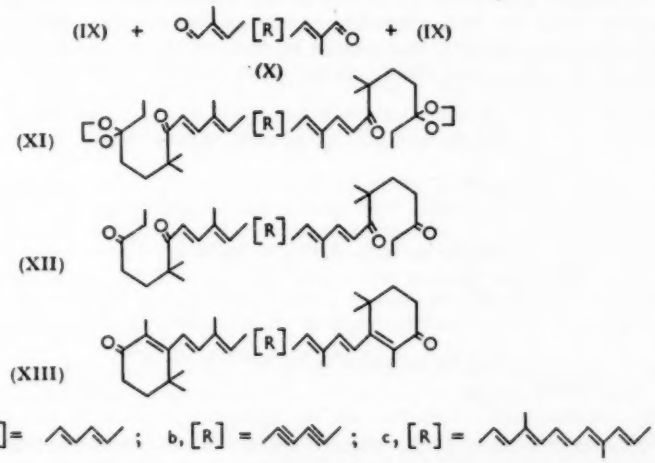
[1] Lederer, *Compt. rend.*, 1935, **201**, 300; Lederer and Moore, *Nature*, 1936, **137**, 996.
[2] Goodwin and Taha, *Biochem. J.*, 1950, **47**, 244; 1951, **48**, 513; cf. Goodwin, *ibid.*, 1956, **63**, 481.
[3] Heilbron and Lythgoe, *J.*, 1936, 1376; Karrer and Rutschmann, *Helv. Chim. Acta*, 1944, **27**, 1691.
[4] Tischer, *Z. physiol. Chem.*, 1938, **251**, 109; 1939, **260**, 257.
[5] Wallcave and Zechmeister, *J. Amer. Chem. Soc.*, 1953, **75**, 4495; cf. *ibid.*, 1956, **78**, 3188.
[6] Ganguly, Krinsky, and Pinckard, *Arch. Biochem. Biophys.*, 1956, **60**, 345.

a product which was not isolated, but was claimed as echinenone from its spectral and chromatographic properties. From the complex mixture of substances formed on treatment of β-carotene with *N*-bromosuccinimide in chloroform containing 1% of alcohol, Petracek and Zechmeister [7] isolated mono- and di-oxo-derivatives in 5 and 1% yield respectively. They presented convincing evidence for the formulation of these products as (I) and (V). The monoketone they identified with echinenone and the diketone with canthaxanthin, a pigment first isolated by Haxo [8] from the edible mushroom *Cantharellus cinnabarinus* and subsequently found in some mutant strains of the bacterium *Corynebacterium michiganense*.[9] In this paper we report unambiguous rational syntheses of both carotenoids. A different approach to canthaxanthin has been briefly outlined by Isler *et al.*[10]

Reaction of the half-ester acid chloride (VI) of αα-dimethylglutaric acid with ethylcadmium furnished the keto-ester (VII). This readily exchanged the ethylenedioxy-group



with 2-ethylenedioxybutane, to give the ester (VIII; Y = Me) which was hydrolysed to the corresponding acid (VIII; Y = H). Treatment of the latter with methyl-lithium gave the methyl ketone (IX), which was characterised by the formation of a mono-semicarbazone and, after initial hydrolysis, a bis-2 : 4-dinitrophenylhydrazone.



To establish the validity of the method envisaged for the introduction of the trimethyl*cyclo*hexenone ring system into polyenes, the following synthesis was carried out. Condensation of the tetraenedial [11] (Xa) with the methyl ketone (IX) in the presence of aluminium

[7] Petracek and Zechmeister, *J. Amer. Chem. Soc.*, 1956, **78**, 1427; *Arch. Biochem. Biophys.*, 1956, **61**, 137; cf. Entschel and Karrer, *Helv. Chim. Acta*, 1958, **41**, 402.
[8] Haxo, *Botan. Gaz.*, 1950, **112**, 228.
[9] Saperstein and Starr, *Biochem. J.*, 1954, **57**, 273.
[10] Isler, Montavon, Rüegg, Saucy, and Zeller, *Verh. Naturforsch. Ges. Basel*, 1956, **67**, 379; Isler, Guex, Lindlar, Montavon, Rüegg, Ryser, Saucy, and Schwieter, *Chimia* (*Switz.*), 1958 **12**, 89.
[11] Warren and Weedon, preceding paper.

tert.-butoxide gave the diketone (XIa) which was hydrolysed to the tetraketone (XIIa). [The diacetylenic analogue (XIIb) was similarly prepared from (Xb).[12]] On treatment with methanolic potassium hydroxide the tetraketone (XIIa) underwent the expected cyclisation to give the octaenedione (XIIIa).

The methyl ketone (IX) was then condensed with crocetin-dial [13] (Xc) in the presence of potassium hydroxide, and gave the nonaenedione (XIc) in 62% yield. Removal of the protecting groups by treatment with acetone and toluene-*p*-sulphonic acid afforded the tetraketone (XIIc), in 72% yield, which was cyclised with alkali to give canthaxanthin (XIIIc = V) in 33% yield.

Similarly condensation of β-*apo*-2-carotenal [14] (XIV) with the methyl ketone (IX) gave (32%) the decaene ketone (XV) which was hydrolysed to the diketone (XVI) in 46% yield. Cyclisation with alkali occurred readily and furnished echinenone (I) in 83% yield. In a

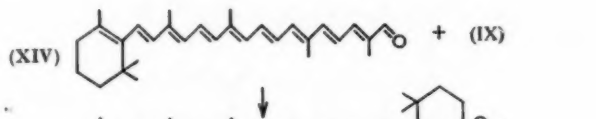
TABLE 1. *Light absorption of polyene-ketones in benzene.*

(Max. in mμ; ε × 10^{-3} in parentheses.)

XIa	449 (78)	428 (85)	XV	484 (120)
XIIa	450 (87)	423 (89)	XVI	483 (121)
XIIIa	—	425 (71)	I	472 (115)
			Natural echinenone [2]	466—468
XIc	518 (116)	485 (128)	,, aphanin [4]	472
XIIc	520 (121)	485 (130)		
XIIIc = V	—	480 (118)		
Natural canthaxanthin [7]	—	480 (118)		

mixed chromatogram the product did not separate from the main carotenoid of the blue alga *Anabaena cylindrica*.

The visible-light absorption properties of the polyene ketones mentioned above are summarised in Table 1. It is noteworthy that the fine structure typical of the spectra of the majority of carotenoids, and present in those of the acyclic ketones, is lacking in the spectra of the natural and the synthetic *cyclo*hexenones.



Some important features of the infrared spectra of the polyene ketones are indicated in Table 2. There are significant differences between the bands due to the conjugated carbonyl group in the *cyclo*hexenones and in the related acyclic ketones. In the former, which perforce have an *s-trans*-configuration about the bond joining the carbonyl group and the polyene chain, absorption is at lower frequencies and of much greater intensity (per C=O group) than in the latter. This lends considerable support to the suggestion made in the previous paper that polyene ketones with a bulky terminal group adopt an *s-cis*-configuration.

[12] Ahmad and Weedon, *J.*, 1953, 3286.
[13] Isler, Gutman, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.
[14] Karrer and Solmssen, *ibid.*, 1937, **20**, 682; Karrer, Solmssen, and Gugelmann, *ibid.*, p. 1020.

TABLE 2. *Infrared light absorption of polyene ketones* (KBr *discs or, where indicated,* $CHCl_3$ *solutions*).

(Frequencies in cm.$^{-1}$; relative intensity in parentheses.)

	Unconjug. C=O stretching	Conjug. C=O stretching	Conjug. C=C stretching region				CH out-of-plane deformation region of conjug. *trans*-CH=CH		
XIa		1668s	1603m	1569vs	1535m		1004m	989s	
XIc		1672s 1674 (387) *		1584s	1546vs		1006ms	983s	968s
XV		1669s		1574vs	1550vs	1512s	1003s	985s	964vs
XIIa	1709s	1669s	1607m	1566vs	1538m		1004m	988s	
XIIb	1706s	1671s		1586vs			1001m	986s	970w
XIIc	1708s 1715 (~660) *	1671s 1672 (~395) *		1582s	1547vs		1004ms	980s	968s
XVI	1709m	1667m	1600w	1575s	1550s	1506s	1003m		966s
XIIIa		1652vs	1610m	1563s	1538w			991vs	966w
V		1658vs 1651 (940) *	1608w	1581m	1555s		998m		966s
I		1657s 1655 (440) *			1550m		1003m		966vs

* In $CHCl_3$; vs, very strong; s, strong; ms, medium strong; m, medium; w, weak.

EXPERIMENTAL

(See notes preceding the Experimental section to Part VI.)

4-Cyano-2 : 2-dimethylbutanal [15] (with N. F. HOLYER).—A styrene-type quaternary ammonium anion-exchange resin [Amberlite resin, IRA-400 (OH), Rohm and Haas Co., Phil., U.S.A., B.D.H., Poole, Eng.] was steeped overnight in 5% aqueous sodium hydroxide, then washed with water and finally with acetone.

Acrylonitrile (150 g.) was added slowly to a well-stirred and cooled (ice) mixture of *iso*-butyraldehyde (200 g.) and the pre-treated ion-exchange resin (54 g.). By regulating the rate of addition the temperature of the mixture was kept at 50—55°. After the addition of the acrylonitrile, the mixture was warmed to 70° for 150 min. The mixture was then cooled and filtered. The filtrate was dried (Na_2SO_4) and distilled to give the cyano-aldehyde (200 g.), b. p. 79—81·5°/0·4 mm., n_D^{23} 1·4381 (Tschudi and Schinz [16] give b. p. 70—75°/0·1 mm., n_D^{20} 1·4349).

αα-Dimethylglutaric Acid.—The above cyano-aldehyde (200 g.) was slowly added to a mixture of 65% nitric acid (330 ml.) and concentrated sulphuric acid (50 ml.) at 60°. By adjustment of the rate of addition, and occasional cooling in ice, the temperature of the mixture was kept at 70—75°. When the addition of the cyano-aldehyde was complete (3 hr.), the solution was kept at 70—75° for a further hour. The mixture was cooled and diluted with ice-water (200 g.), and the precipitated product filtered off. Recrystallisation from water gave αα-dimethylglutaric acid (120 g.), m. p. 80—82° (Tiemann [17] gives m. p. 85°; Wendt [18] gives m. p. 78°).

Dimethyl αα-Dimethylglutarate.—A solution of αα-dimethylglutaric acid (160 g.) and concentrated sulphuric acid (8 ml.) in methanol (2 l.) was refluxed for 16 hr., then cooled. Excess of solid sodium hydrogen carbonate was added and the methanol was distilled off. The residual oil in ether (600 ml.) was washed with water and dried (Na_2SO_4). Distillation gave dimethyl αα-dimethylglutarate (120 g.), b. p. 117—119°/20 mm., n_D^{23} 1·4281 (Blaise [19] gives b. p. 215°).

Methyl Hydrogen αα-Dimethylglutarate.—A solution of dimethyl αα-dimethylglutarate (106 g.) and potassium hydroxide (35 g.) in methanol (650 ml.) was kept at 20° for 16 hr. The mixture was refluxed for 2 hr., then cooled and evaporated to dryness under reduced pressure. The solid residue was treated with the theoretical quantity of 2N-hydrochloric acid, and the liberated half-ester was extracted with ether. The ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. Distillation of the residue from a

[15] Cf. Howk and Langkammerer, U.S.P. 2,579,580.
[16] Tschudi and Schinz, *Helv. Chim. Acta*, 1950, **33**, 1865.
[17] Tiemann, *Ber.*, 1900, **33**, 2942.
[18] Wendt, *Ber.*, 1941, **74**, 1242.
[19] Blaise, *Bull. Soc. chim. France*, 1899, **21**, 626.

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Kon flask gave an oil (b. p. 98—99°/0·05 mm., n_D^{22} 1·4391) which readily crystallised. Recrystallisation from light petroleum gave *methyl hydrogen αα-dimethylglutarate* (76 g.) as needles, m. p. 43·5—45·0° (Found: C, 54·75; H, 8·15. $C_8H_{14}O_4$ requires C, 55·15; H, 8·1%).

Methyl 2 : 2-*Dimethyl-5-oxoheptanoate* (VII).—The preceding methyl half-ester (76 g.) was dissolved in thionyl chloride (120 ml.), and the solution kept at 20° for 3 days. After removal of excess of thionyl chloride at reduced pressure, the residual acid chloride, in benzene (300 ml.), was slowly added to a stirred solution of ethylcadmium (from 100 g. of ethyl bromide) in benzene (1 l.). The mixture was refluxed for 50 min., then cooled. Ice and 2N-sulphuric acid (250 ml.) were added. Isolation of the product with benzene in the usual way and fractional distillation (Stedman column, 15 × 2 cm.; partial take-off head) gave the above *keto-ester* (52 g.), b. p. 74—75°/0·7 mm., n_D^{21} 1·4352 (Found: C, 64·35; H, 9·8. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%). A solution of the keto-ester (200 mg.), semicarbazide hydrochloride (300 mg.), and crystalline sodium acetate (0·5 g.) in aqueous ethanol (1 : 1; 4 ml.) was kept at 0° for 14 days. Water (2 ml.) was added and the mixture was kept at 0° for 1 hr. Collection of the solid and recrystallisation from aqueous methanol gave the *semicarbazone* (240 mg.) as plates, m. p. 123—124° (Found: C, 54·4; H, 8·55. $C_{11}H_{21}O_3N_3$ requires C, 54·3; H, 8·7%).

2 : 2-*Dimethyl-5-oxoheptanoic Acid.*—Methyl 2 : 2-dimethyl-5-oxoheptanoate (1·0 g.), 5N-sodium hydroxide (1·2 ml.), and methanol (1·5 ml.) were refluxed together for 30 min. Water (1·0 ml.) was added and refluxing was continued for 60 min. The mixture was cooled and evaporated almost to dryness. Water (1·0 ml.) was added and the evaporation was repeated. A solution of the wet residue in water (5 ml.) was acidified with 2N-hydrochloric acid, and the liberated organic acid was isolated with ether. Crystallisation from pentane, containing a trace of ether, gave the keto-acid (0·6 g.), m. p. 24—26·5°. The 2 : 4-*dinitrophenylhydrazone*, crystallised from aqueous methanol, had m. p. 112—126° (Found: C, 50·85; H, 5·8. $C_{15}H_{20}O_6N_4$ requires C, 51·15; H, 5·7%). The *benzylammonium salt* crystallised from ethyl acetate–light petroleum (9 : 1) as needles, m. p. 75° (Found: C, 68·55; H, 9·0. $C_{16}H_{25}O_3N$ requires C, 68·8; H, 9·0%). When kept at 10^{-6} mm. the salt lost benzylamine.

Methyl 5-*Ethylenedioxy*-2 : 2-*dimethylheptanoate* (VIII; Y = Me).—A mixture of methyl 2 : 2-dimethyl-5-oxoheptanoate (42 g.), 2-ethylenedioxybutane (110 g.), and toluene-*p*-sulphonic acid (0·2 g.) was refluxed through a fractionating column (Stedman, 15 × 2 cm.) under a partial take-off head. At intervals during 7 hr. small portions of the distillate were withdrawn until a total of 37 ml. had been collected. The mixture was cooled, washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and distilled through the same fractionating column, to give the *ethylenedioxy-ester* (32 g.), b. p. 90—92°/1·0 mm., n_D^{21} 1·4438 (Found: C, 63·25; H, 9·8. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·65%).

5-*Ethylenedioxy*-2 : 2-*dimethylheptanoic Acid* (VIII; Y = H). The above ethylenedioxy-ester (32 g.), 5N-sodium hydroxide (28·0 ml.), and methanol (35 ml.) were refluxed together for 30 min. Water (22 ml.) was added and the mixture was refluxed for 1 hr. The mixture was cooled and evaporated almost to dryness. Water (15 ml.) was added, and most of the solvent was again evaporated. A solution of the residue in water (100 ml.) was cooled to 0° and shaken with ether (250 ml.) whilst 2N-hydrochloric acid was added until the mixture was almost neutral. The organic layer was separated, and the aqueous phase was extracted with ether (50 ml. × 3). The combined ethereal solutions were dried ($MgSO_4$) and evaporated. Crystallisation of the residual oil from pentane, containing a trace of ether, gave the ethylenedioxy-acid (28 g.) as prisms, m. p. 15—17°, mixed m. p. with the keto-acid described above, 0—15°.

Treatment of the ethylenedioxy-acid with Brady's reagent gave the 2 : 4-dinitrophenylhydrazone of the corresponding keto-acid, m. p. and mixed m. p. 111—126°.

Addition of benzylamine (0·5 ml.) in benzene (0·5 ml.) to the ethylenedioxy-acid (0·5 g.) gave a pale yellow solid. Recrystallisation from ethyl acetate–light petroleum (9 : 1) gave the *benzylammonium salt* (0·4 g.), m. p. 88—88·5°, mixed m. p. with the corresponding derivative of the keto-acid 66—68° (Found: C, 66·85; H, 9·35. $C_{18}H_{29}O_4N$ requires C, 66·85; H, 9·05%).

6-*Ethylenedioxy*-3 : 3-*dimethyloctan*-2-*one* (IX).—5-Ethylenedioxy-2 : 2-dimethylheptanoic acid (27 g.) in ether (100 ml.) was slowly added to a vigorously stirred solution of methyllithium (6·1 g.) in ether (250 ml.). The mixture was refluxed for 90 min., then cooled to 0°. Cold water (100 ml.) was added. Isolation of the product with ether in the usual way and distillation gave the *ethylenedioxy-ketone* (22 g.), b. p. 78—84°/0·5 mm., n_D^{21} 1·4508 (Found:

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C, 67·55; H, 10·9. $C_{12}H_{22}O_3$ requires C, 67·25; H, 10·35%). The *semicarbazone* (92% yield) crystallised from aqueous methanol as plates, m. p. 119·5° (Found: C, 57·35; H, 9·3. $C_{13}H_{25}O_3N_3$ requires C, 57·55; H, 9·3%). Treatment of the ethylenedioxy-ketone with Brady's reagent gave the derivative of the corresponding diketone in 89% yield. Crystallisation from dioxan–methanol–water (1 : 1 : 1) gave 3 : 3-*dimethyloctane*-2 : 6-*dione* 2 : 4-*dinitrophenylhydrazone* as orange needles, m. p. 179—185° (Found: C, 49·9; H, 5·15. $C_{22}H_{26}O_8N_8$ requires C, 49·8; H, 4·95%).

3 : 24-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 17 : 21 : 21-*hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-7 : 20-*dione* (XIa).—A mixture of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraenedial (206 mg.), 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (5·0 g.) and aluminium *tert.*-butoxide (1·0 g.) in benzene (10 ml.) was heated under reflux for 20 hr., then cooled and diluted with benzene (100 ml.). The solution was washed successively with 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. Excess of 6-ethylenedioxy-3 : 3-dimethyloctan-2-one was distilled off at 60° (bath-temp.)/10^{-6} mm. Chromatography of the residue in benzene on alumina, isolation of the main yellow band, and crystallisation from benzene–light petroleum gave the hexaenedione (162 mg.) as yellow needles, m. p. 143—146°.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-3 : 7 : 20 : 24-*tetraone* (XIIa).—A solution of the preceding hexaenedione (136 mg.) in acetone (60 ml.) containing toluene-*p*-sulphonic acid (20 mg.) was refluxed for 90 min. The mixture was cooled, diluted with benzene (100 ml.), washed with saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from benzene–light petroleum gave the *tetraone* (105 mg.) as yellow needles, m. p. 105—107° (Found: C, 78·0; H, 9·4. $C_{32}H_{46}O_4$ requires C, 77·7; H, 9·35%).

3 : 10-*Dimethyl*-1 : 12-*di*-(2 : 6 : 6-*trimethyl*-3-*oxo*cyclo*hex*-1-*enyl*)*dodeca*-1 : 3 : 5 : 7 : 9 : 11-*hexaene* (XIIIa).—A solution of the above hexaenetetraone (36 mg.) in 10% methanolic potassium hydroxide (50 ml.) and benzene (5 ml.) was refluxed for 2½ hr. The mixture was cooled, diluted with benzene (100 ml.), washed successively with water, 0·5N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina gave two bands, A and B, which were eluted with benzene. The solution from the more readily eluted band A was evaporated, and the residue was crystallised from light petroleum, to give the *dione* (10·5 mg.) as orange-yellow needles, m. p. 203° (Found: C, 83·3; H, 9·5. $C_{32}H_{42}O_2$ requires C, 83·8; H, 9·25%). The solution from band B was evaporated, and the residue was recycled to give a further 3 mg. of the required dione (total yield 13·5 mg., 40%).

3 : 24-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 17 : 21 : 21-*hexamethylhexacosa*-8 : 10 : 16 : 18-*tetraene*-12 : 14-*diyne*-7 : 20-*dione* (XIb).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial [19] (100 mg.), 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (2 ml.), and aluminium *tert.*-butoxide (1·0 g.) in benzene (10 ml.) was boiled for 20 hr. and then cooled. Isolation of the product in the usual way gave the *dione*, which crystallised from benzene–light petroleum in yellow prisms (56 mg.), 114—115° (Found: C, 74·8; H, 8·9. $C_{36}H_{50}O_6$ requires C, 74·7; H, 8·7%), $\lambda_{max.}$ (in *n*-hexane) 403, 373, 347, and 254 mμ ($\varepsilon \times 10^{-3}$, 50·4, 51·9, 42·1, and 16·7 respectively).

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 16 : 18-*tetraene*-2 : 14-*diyne*-3 : 7 : 20 : 24-*tetraone* (XIIb).—A solution of the preceding dione (42 mg.) and toluene-*p*-sulphonic acid (20 mg.) in acetone (24 ml.) was boiled for 90 min. Isolation of the product in the usual way gave the *tetraone* which crystallised from benzene–light petroleum as yellow prisms (8 mg.), m. p. 127—128° (Found: C, 78·45; H, 8·2. $C_{32}H_{42}O_4$ requires C, 78·35; H, 8·65%), $\lambda_{max.}$ (in *n*-hexane) 402, 372, 346, and 254 mμ ($\varepsilon \times 10^{-3}$, 45·0, 46·0, 37·6, and 14·9 respectively).

3 : 30-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 14 : 19 : 23 : 27 : 27-*octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-7 : 26-*dione* (XIc).—A suspension of crocetindial [20] (253 mg.) in a mixture of 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (4·2 ml.) and 5% ethanolic potassium hydroxide (6·0 ml.) was kept at 20°, and shaken occasionally, for 4 hr. The mixture was then refluxed for 15 min., cooled, diluted with benzene (100 ml.), washed successively with water, 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. The oily residue, consisting mainly of excess of the initial methyl ketone, was diluted with light petroleum (40 ml.) and kept overnight at 0°.

[20] Isler, Gutmann, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.

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The deep-red leaflets (362 mg.), m. p. 170—172°, which had separated were collected and recrystallised from benzene–light petroleum to give the *nonaenedione* as deep-red leaflets, m. p. 174° (Found: C, 76·5; H, 9·85. $C_{44}H_{64}O_6$ requires C, 76·7; H, 9·35%).

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27-*Octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-3 : 7 : 26 : 30-*tetraone* (XIIc).—A solution of the preceding nonaenedione (310 mg.) in acetone (50 ml.) containing toluene-*p*-sulphonic acid (20 mg.) was refluxed for 60 min., then cooled, diluted with benzene (150 ml.), washed with saturated sodium hydrogen carbonate solution and water, and dried (Na_2SO_4). Evaporation, and crystallisation of the residue from benzene–light petroleum, gave the *nonaenetetraone* (174 mg.) as deep-red plates, m. p. 174° (Found: O, 10·5. $C_{40}H_{56}O_4$ requires O, 10·65%). The mother-liquors from the above crystallisations were evaporated to dryness and the residue dissolved in acetone (25 ml.) containing toluene-*p*-sulphonic acid (10 mg.). In 3 days at 0°, the solution deposited deep-red crystals which recrystallised from benzene–light petroleum to give a further 23 mg. of the nonaenetetraone (total yield 197 mg., 72%).

Canthaxanthin (V).—A suspension of the preceding nonaenetetraone (100 mg.) in 10% methanolic potassium hydroxide (150 ml.) and benzene (20 ml.) was refluxed for 2 hr. (A homogeneous solution was obtained after 30 min.) The mixture was cooled, diluted with benzene (250 ml.), washed successively with water, 2N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene solution on grade III alumina gave two red bands, A and B, which were eluted with benzene. The solution from the more readily eluted band A was evaporated to dryness and the residue crystallised from benzene–light petroleum to give canthaxanthin (23 mg.) as red prisms, m. p. 215° (Found: O, 5·7. $C_{40}H_{52}O_2$ requires O, 5·65%). The solution from band B was evaporated to dryness and the residue recycled to give a further 8 mg. of canthaxanthin (total yield 31 mg., 33%). No study was made of the optimum conditions for the cyclisation. (For natural canthaxanthin, Petracek and Zechmeister [7] give m. p. 213°.)

3-*Ethylenedioxy*-6 : 6 : 10 : 14 : 19 : 23-*hexamethyl*-25-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)-*pentacosa*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaen*-7-*one* (XV).—A suspension of β-*apo*-2-carotenal (102 mg.) in a mixture of 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (4·2 ml.) and 5% ethanolic potassium hydroxide (4·2 ml.) was kept at 20°, and shaken occasionally, for 6½ hr. The mixture was then refluxed for 15 min., cooled, diluted with benzene (60 ml.), washed successively with water, 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. The excess of the initial methyl ketone was distilled off at 60° (bath-temp.)/10^{-6} mm. Chromatography of the residue from light petroleum on grade III alumina gave one main red band which was eluted with benzene–light petroleum (1 : 1). Evaporation and crystallisation of the glass-like residue from light petroleum gave the *nonaenone* (47·5 mg.) as violet needles, m. p. 124—125° (Found: O, 7·9. $C_{42}H_{60}O_3$ requires O, 7·85%).

6 : 6 : 10 : 14 : 19 : 23-*Hexamethyl*-25-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)*pentacosa*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-3 : 7-*dione* (XVI).—A solution of the preceding nonaenone (86 mg.) in acetone (50 ml.) containing toluene-*p*-sulphonic acid (10 mg.) was kept overnight at 20°. The mixture was then refluxed for 30 min., cooled, diluted with benzene (60 ml.), washed successively with saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from methanol–light petroleum gave the *nonaenedione* (27 mg.) as dull red prisms, m. p. 124° (Found: O, 6·0. $C_{40}H_{56}O_2$ requires O, 5·65%). The mother-liquors from the above crystallisations were combined and evaporated. Chromatography of the residue from light petroleum on grade III alumina gave one main red band which was developed with benzene–light petroleum (b. p. 60—80°) and eluted with benzene. Evaporation and crystallisation of the resdue from light petroleum gave a further 10·5 mg. of the nonaenedione (total yield 37 mg., 46%).

Echinenone (I).—A solution of the preceding nonaenedione (28 mg.) in 10% methanolic potassium hydroxide (35 ml.), containing benzene (5 ml.), was refluxed for 150 min. The product crystallised out from the hot mixture as violet plates, m. p. 186—187°. Recrystallisation from benzene–methanol gave echinenone (23 mg.) as violet plates, m. p. 187° (Found: C, 87·25; H, 10·05. $C_{40}H_{54}O$ requires C, 87·2; H, 9·9%). (For natural echinenone, Lederer [1] gives m. p. 178—179° and 192°; for synthetic echinenone Petracek and Zechmeister [7] give m. p. 175—178°.)

Dried *Anabaena cylindrica* (1·9 g.) was extracted at 20° with methanol (25 ml.) for 4 days,

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then with ether (25 ml.) for 5 hr., and again with ether (30 ml.) for 16 hr. The extracts were combined and evaporated. Chromatography of the residue on alumina (grade IV) first from benzene and then from light petroleum (b. p. 40—60°) gave a reddish-brown band, $\lambda_{max.}$ 472 mμ (492 mμ in CS_2). In a mixed chromatogram this band did not separate from synthetic echinenone.

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805. *Some Nitric Oxide Complexes of Iron and Copper.*

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The magnetic suceptibilities and absorption spectra of the complex ions $[Fe(H_2O)_5NO]^{2+}$, $[Fe(NH_3)_5NO]^{2+}$, and $[Fe(C_2H_5{\cdot}OH)_5NO]^{2+}$ have been measured. It is concluded that these paramagnetic species have sp^3d^2-outer-orbital bonding involving co-ordination of the nitrosyl (NO^+) ion to the metal atom. $[Fe(CN)_5NO]^{2-}$, which involves co-ordination of nitric oxide to the metal atom by two electrons only, $[Cu(C_2H_5{\cdot}OH)_3NO]^{2+}$, and $Fe(NO)_4$ have also been studied.

The Penta-aquonitrosyliron(I) *Ion*, $[Fe(H_2O)_5NO]^{2+}$; *"Brown-ring" Compounds.*—Aqueous solutions of ferrous salts absorb nitric oxide [1] to give dark brown, unstable substances, sometimes known as the "brown-ring" compounds since they are also formed in the familiar qualitative tests for nitrates. The first quantitative studies on these compounds were made by Manchot and his co-workers,[2-5] who studied the equilibrium

$$Fe_{aq}^{2+} + NO \rightleftharpoons Fe(NO)_{aq}^{2+}$$

in chloride and sulphate solutions [2,3,4] over a range of temperatures and evaluated [3] the heats of reaction in aqueous solution (11·9 kcal./mole). Electrolysis of the solutions showed that nitric oxide was bound in a cationic complex.[5] Measurements of the absorption spectra of solutions [6] gave results independent of the nature of the anion and in addition, since we find that brown-ring compounds can be prepared in perchlorate solution, it seems unlikely that the cation is other than an octahedral penta-aquonitrosyliron(I) ion, $[Fe(H_2O)_5NO]^{2+}$.

Manchot isolated some of the nitrosyl compounds as rather ill-defined solids: the sulphate as $Fe(NO)SO_4$ and $2Fe(NO)SO_4,13H_2O$,[7] the selenate as $Fe(NO)SeO_4,4H_2O$,[5] and the phosphate as $Fe(NO)HPO_4$.[8] Much work has been done on the decomposition products in acidic, neutral, and alkaline solutions of the brown-ring compounds; [9-13] this

[1] Priestley, "Experiments and Observations on Different Kinds of Air," Thomas Pearson, Birmingham, 1790, Vol. I, p. 328.
[2] Manchot, *Annalen*, 1910, **372**, 179.
[3] Manchot and Haunschild, *Z. anorg. Chem.*, 1924, **140**, 22.
[4] Manchot and Zechentmayer, *Annalen*, 1906, **350**, 368.
[5] Manchot and Linckh, *Z. anorg. Chem.*, 1924, **140**, 37.
[6] (*a*) Schlesinger and Van Volkenburgh, *J. Amer. Chem. Soc.*, 1929, **51**, 1323; (*b*) Schlesinger and Salathe, *ibid.*, 1923, **45**, 1863.
[7] Manchot and Huttner, *Annalen*, 1910, **372**, 153.
[8] Manchot, *Annalen*, 1910, **375**, 308.
[9] (*a*) Dunstan and Dymond, *J.*, 1887, **51**, 646; (*b*) Usher, *Z. phys. Chem.*, 1908, **62**, 622.
[10] (*a*) Divers and Haga, *J.*, 1885, **47**, 361; (*b*) Huffner, *Z. phys. Chem.*, 1907, **59**, 416.
[11] (*a*) Kohlschutter and Sazanoff, *Ber.*, 1911, **44**, 1423; (*b*) Cambi and Clerici, *Atti R. Accad. Lincei*, 1929, **9**, 519.
[12] (*a*) Manchot, *Ber.*, 1914, **47**, 1614; (*b*) Cambi and Gagnasso, *Atti R. Accad. Lincei*, 1930, **11**, 133.
[13] Tarte, *Ind. chim. Belg.*, 1952, **17**, 42.

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was briefly reviewed by Tarte,[13] who also carefully and thoroughly investigated the decomposition products of slightly acidic ferrous sulphate–nitric oxide complexes. Tarte found that little or no oxidation of the ferrous ion had taken place after removal of nitric oxide from the solutions under reduced pressure; all of the ferrous sulphate was regenerated. It must therefore be assumed that previous workers who claimed that oxidation did take place must have used nitric oxide containing traces of nitrogen dioxide. In alkaline or neutral solution the ferrous is readily oxidised to the ferric state, and it is not surprising that such partial oxidation occurred, with reduction of nitric oxide to nitrogen and nitrous oxide; according to Cambi,[14] some hyponitrite occurs in the residual alkaline liquors, but this could not be confirmed.[13]

We measured the magnetic susceptibility of aqueous solutions of the ferrous sulphate–nitric oxide complex over a wide range of concentrations. By using Manchot and Haunschild's values [3] of the equilibrium constant for the reaction, which we now write as

$$[Fe(H_2O)_6]^{3+} + NO \rightleftharpoons [Fe(H_2O)_5NO]^{2+} + H_2O$$

we obtained the values given in the last column of Table 1. These show that the complex has three unpaired electrons. The infrared spectra in the N–O stretching region of the brown-ring compounds both in the solid state and in aqueous solutions (Table 2) show frequencies in the region 1730—1850 cm.$^{-1}$, which is characteristic of nitric oxide in complexes derived by co-ordination from NO^+.[15] Ferrous nitrosyl selenate absorbs at 1853 cm.$^{-1}$.[16]

The brown-ring complex being assumed octahedral with only water and nitric oxide as ligands, the above facts conclusively eliminate the formulations as (*a*) an inner-orbital complex (d^2sp^3) with nitric oxide donating three electrons to the metal, since here the complex would be diamagnetic and of the form $[Fe^{II}(H_2O)_5NO]^{3+}$ and would give a ferric

TABLE 1. *Magnetic measurements on aqueous solution of* $[Fe(H_2O)_5NO]SO_4$ *at* 293° K.

Susceptibility values (χ) are in c.g.s. units × 10^6.

$[Fe^{2+}]$ (moles/l.)	0·91	0·78	0·53	0·42	0·25	0·19
χ_g{$[Fe(H_2O)_5NO]SO_4$} *	24·7	24·7	22·8	24·1	24·9	23·7
χ_M †	6700	6700	6200	6550	6770	6440
$\mu_{eff.}$ (B.M.)	3·97	3·97	3·80	3·90	3·99	3·88

* Assuming $\chi_g(FeSO_4,7H_2O) = 41·5 \times 10^{-6}$ c.g.s. units.
† For Fe atom fully corrected for diamagnetism of ligands and anion.

TABLE 2. *Infrared spectra of iron and copper nitrosyl compounds in* N–O *region* (cm.$^{-1}$)

Where no solvent is given the value refers to the solid state.

$[Fe(H_2O)_5NO]SO_4$	1765(s) (3% H_2SO_4)	$[Fe(NH_3)_5NO]SO_4$	1745(m)
$[Fe(H_2O)_5NO]Cl_2$	1795(s) (3% HCl)	$[Fe(C_2H_5{\cdot}OH)_5NO]Cl_3$	1775(s) ($C_2H_5{\cdot}OH$)
$[Fe(H_2O)_5]SeO_4$	1815(s) (3% H_2SeO_4)	$Fe(NO)_2NO$	1810(vs), 1730(s), 1140(m)
$2FeSO_4{\cdot}NO,13H_2O$	1845(s)		
$FeHPO_4NO,xH_2O$	1738(s) (CCl_4)	$[Cu(C_2H_5{\cdot}OH)_2NO]Cl_2$	1854 ($C_2H_5{\cdot}OH$)
$[Fe(NH_3)_5NO]Cl_2$	1754(s)	$[Cu(C_2H_5{\cdot}OH)_2NO]Br_2$	1848 ($C_2H_5{\cdot}OH$)

salt on decomposition, which does not occur;[13] (*b*) an inner-orbital complex with nitric oxide donating two electrons, since such a complex $[Fe^{II}(H_2O)_5NO]^{2+}$ would have one unpaired electron and should react with potassium cyanide to give $K_3[Fe^{II}(CN)_5NO]$ (see below), which it does not; (*c*) an inner- or outer-orbital complex involving hyponitrite bridging, since no absorption is found in the region ~1200 cm.$^{-1}$ (cf. ref. 17); (*d*) an outer-orbital complex (sp^3d^2) with nitric oxide donating two electrons to the metal, since in this case, $[Fe^{II}(H_2O)_5NO]^{2+}$, the magnetic susceptibility would be the same as that of the ferrous ion.

[14] Cambi, *Z. anorg. Chem.*, 1941, **247**, 22.
[15] Lewis, Irving, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 32.
[16] Hieber and Jahn, *Z. Naturforsch.*, 1958, **13***b*, 196.
[17] Griffith, Lewis, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 38.

The only acceptable formulation is that of an outer-orbital complex (sp^3d^2), $[Fe^{I}(H_2O)_5NO]^{2+}$ with the nitric oxide donating three electrons to the ferrous ion. The N–O stretching frequency in such a complex might well be expected to lie in the region 1730—1850 cm.$^{-1}$ (where inner-orbital nitric oxide complexes absorb) as, although no π-bonding in the metal–NO bond is possible, the outer-orbital bonding will be more polar in character than the inner-orbital bonding which occurs in the diamagnetic nitric oxide complexes. In addition, this formulation indicates a magnetic moment corresponding to three unpaired electrons and would be in keeping with the regeneration of the ferrous ion on removal of nitric oxide, in accordance with the observations.

The brown colour of the complexes is attributable to charge-transfer spectra; since the iron atom is formally in the +1 oxidation state a comparison of ligand-field bands with those in other iron complexes is not possible. Table 3 contains values of the extinction

TABLE 3. *Absorption spectra in the near infrared and visible regions.*

Complex	ε	Wavelength		Complex	ε	Wavelength	
$[Fe(H_2O)_5NO]SO_4$ ...	38	385 mμ	17,100 cm.$^{-1}$	$[Cu(C_2H_5{\cdot}OH)_2NO]Cl_2$	51·1	805 mμ	12,450 cm.$^{-1}$
$[Fe(C_2H_5{\cdot}OH)_5NO]Cl_2$	15·7	810 ,,	12,400 ,,		309·1	565 ,,	17,700 ,,

coefficient at the various maxima for the solution of the iron and copper complexes. The absorption spectrum of $[Fe(EtOH)_5NO]Cl_3$ in the region 500—800 mμ is similar to that of $[Fe(EtOH)_6]Cl_2$, as expected from the above considerations.

The Pentamminonitrosyliron(I) *Ion*, $[Fe(NH_3)_5NO]^{2+}$.—The very unstable chloride and sulphate of this ion were made by Weitz and Muller.[18] The infrared spectra, measured in solution, are similar to those of the brown-ring compounds. The determination of the magnetic moment was not possible owing to the presence of a trace of a ferromagnetic impurity, which proved impossible to eliminate. It seems reasonable to assume, however, that the ion is similar to the above aquo-species and that it is $[Fe^{I}(NH_3)_5NO]^{2+}$ and not, as may have been expected, similar to the red salt $[Co(NH_3)_5NO]SO_4$.[17]

The Pentacyanonitrosyliron(II) *Ion*, $[Fe(CN)_5NO]^{3-}$.—Aqueous solutions of $Na_3[Fe(CN)_5NH_3]$ in the presence of a slight excess of acetic acid (to absorb ammonia) absorb either carbon monoxide or nitric oxide to give $Na_3[Fe(CN)_5CO]$ and the ion $[Fe(CN)_5NO]^{3-}$ respectively.[19] The latter cannot be isolated as a salt, but the ratio Fe : NO is unity. Sidgwick [20] suggested that the nitric oxide is bound to the metal by two electrons only, just as the carbon monoxide is bound in the diamagnetic carbonyl cyanide. It is not true, however, that the complex exists in a violet and a yellow form as stated by Sidgwick.

Magnetic-susceptibility measurements at three concentrations in aqueous solution show that the complex has a moment corresponding to slightly less than one unpaired electron (Table 4). Addition of aqueous sodium hydroxide to solutions of the complex in absence of air leads to the ferrous aquo-complex $Na_3[Fe^{II}(CN)_5H_2O]$, while in the presence of air the ferric compound $Na_2[Fe^{III}(CN)_5H_2O]$ is obtained. The action of potassium cyanide in absence of air produces the ferrocyanide. These chemical reactions show clearly that in the nitric oxide complex the iron is ferrous. Although formally the complex could be considered the equivalent of the ions $[Fe(H_2O)_5NO]^{2+}$ and $[Fe(NH_3)_5NO]^{2+}$, it cannot be formed from them by the action of cyanide, differing in this regard from the complex $[Fe(C_2H_5{\cdot}OH)_5NO]^{3+}$ (see below), which produces the nitroprusside ion. This difference is in keeping with Sidgwick's formulation $[Fe^{II}(CN)_5NO]$, the odd electron remaining localised on the ligand in this case, with inner-orbital d^2sp^3 bonding due to the strong ligand-field effect of the cyanide ion.

The Pentaethanolnitrosyliron(III) *Ion*, $[Fe(C_2H_5{\cdot}OH)_5NO]^{3+}$.—This new complex ion is

[18] Weitz and Muller, *Angew. Chem.*, 1950, **62**, 221.
[19] Manchot, Merry, and Worringer, *Ber.*, 1912, **45**, 2869.
[20] Sidgwick, "The Chemical Elements and their Compounds," Oxford University Press, 1950, p. 1360.

obtained by passing dry nitric oxide into anhydrous ethanolic solutions of anhydrous ferric chloride. It is dark green in solution and, like the cupric–nitric oxide complexes discussed below, cannot be isolated as a solid salt. Measurement of the absorption of nitric oxide by

TABLE 4. *Magnetic measurements on aqueous solutions of* $Na_3[Fe(CN)_5NO]$ *at* 295·4° K.

$[Fe(CN)_5NO]^{3-}$ (moles/l.)	$\chi_g(Na_3[Fe(CN)_5NO])$	χ_M *	$\mu_{eff.}$ (B.M.)
0·44	2·66	826	1·41
0·34	2·58	803	1·38
0·20	3·40	1036	1·56

TABLE 5. *Magnetic measurements on ethanolic solutions of* $[Fe(C_2H_5{\cdot}OH)_5NO]Cl_3$ *at* 295·4° K.

$[Fe^{3+}]$ (moles/l.)	$\chi_g\{[Fe(C_2H_5{\cdot}OH)_5NO]Cl_3\}$ †	χ_M *	$\mu_{eff.}$ (B.M.)
0·314	52·6	10,100	4·89
0·135	54·4	10,500	4·98
0·132	55·3	10,600	5·01
0·076	56·7	10,900	5·10
0·065	56·3	10,900	5·08

For Tables 4 and 5, susceptibilities are in c.g.s. units $\times 10^6$.
* For Fe atom, fully corrected for diamagnetism of ligands and cation.
† χ_g for $FeCl_3$ is taken as $86{\cdot}2 \times 10^{-6}$ c.g.s. units.

ferric chloride solutions of different concentrations shows that the ratio NO : Fe is somewhat less than unity, and that in solution there is an equilibrium

$$[Fe(C_2H_5{\cdot}OH)_6]^{3+} + NO \rightleftharpoons [Fe(C_2H_5{\cdot}OH)_5NO]^{3+} + C_2H_5{\cdot}OH.$$

The equilibrium constant and heat of reaction were determined; magnetic measurements over a concentration range indicate a moment corresponding to four unpaired electrons (Table 5). An absorption band at 1775 cm.$^{-1}$ in ethanolic solution is attributed to nitric oxide's donating as NO^+. The compound is decomposed by water; with potassium cyanide traces of $K_2[Fe^{II}(CN)_5NO]$ are formed.

The only structure in keeping with the results is $[Fe^{II}(C_2H_5{\cdot}OH)_5NO]^{3+}$ involving sp^3d^2 outer-orbital bonding. The complex is thus the ferric analogue of the brown-ring compound. The fact that water decomposes the complex, and that aqueous ferric solutions do not absorb nitric oxide, seems to indicate that the ion $[Fe^{II}(H_2O)_5NO]^{3+}$ does not exist in detectable concentration; solutions of the hexammine–iron(III) ion [21] also do not absorb nitric oxide.

Iron Tetranitrosyl, $Fe(NO)_4$.—This compound was made by Manchot and Enk [22] by treating iron pentacarbonyl with nitric oxide under pressure. It is very reactive, forming compounds such as $Fe(NO)SO_4$ with sulphuric acid, $Fe(NO)_2S{\cdot}C_2H_5$ with ethanethiol, etc. Sidgwick suggested (ref. 20, pp. 1373, 1485) that the compound had the structure $[Fe(NO)_3]^-NO^+$; this would account for its non-volatility and would give an inert-gas structure to the metal atom.

Unfortunately the compound is so unstable (it decomposes slowly above 0° even in nitrogen) that it is impossible to measure its magnetism reliably. Infrared spectra of several different preparations of the substance have been obtained, however (Table 2). These show two frequencies in the NO^+ region and one near 1150 cm.$^{-1}$ in the region assigned to nitric oxide donating in complexes as NO^-.[17] This suggests that the compound has the structure (I), with three nitric oxide molecules donating as NO^+ and one as NO^-.

The two higher frequencies are similar to those observed (at 1826 cm.$^{-1}$ and 1763 cm.$^{-1}$) for $Fe(NO)_3Cl$,[16] with which $[Fe^+(NO)_3]NO^-$ is clearly analogous.

[21] Biltz and Birk, *Z. anorg. Chem.*, 1923, **134**, 125.

The tetranitrosyl does not decompose to give a dimer $[Fe(NO)_3]_2$ as might be expected by analogy with the decomposition of $Fe(NO)_3Br$;[23] this must be because nitric oxide has less tendency to act as a bridge group.

The Triethanolnitrosylcopper(I) Ion, $[Cu(C_2H_5{\cdot}OH)_3NO]^{2+}$.—Cupric salts in non-aqueous solvents absorb nitric oxide to give violet complexes [4, 8, 24] which are considerably weaker than those of ferrous iron. Electrolysis shows that the nitric oxide is associated with a copper cation of +2 charge.[25] According to Kohlschutter and Kutscheroff,[24] the ratio NO : Cu in ethanol is 3·6 : 1. Later experiments by Manchot [8] showed that this value was in error and that the ratio NO : Cu was in fact less than unity. We confirmed this observation and determined the equilibrium constant (Table 6) of the reaction which we now write as

$$[Cu(C_2H_5{\cdot}OH)_4]^{2+} + NO \rightleftharpoons [Cu(C_2H_5{\cdot}OH)_3NO]^{2+} + C_2H_5{\cdot}OH.$$

Magnetic measurements on the ethanolic solutions show that the complex is diamagnetic and the infrared spectrum (Table 2) shows that the complex must be formulated with donation by NO^+.

TABLE 6. *Equilibrium constants and heats of reaction in ethanolic solutions.*

$[Fe^{3+}]$ (moles/l.)	Temp. (°K)	p_{NO} (mm.)	V *	K' †	$[Cu^{2+}]$ (moles/l.)	Temp. (°K)	p_{NO} (mm.)	V *	K' ‡
0·034	282·4	740·0	21·3	—	0·05	273·4	742·9	19·1	—
0·017	282·4	740·0	21·0	43·8	0·025	273·4	742·9	20·1	115·0
0·034	294·4	724·1	18·0	—	0·05	283·0	731·9	17·3	—
0·017	294·4	724·1	17·4	196·0	0·025	283·0	731·9	17·0	226·4
0·034	298	705·0	15·2	—	0·05	297·6	696·9	15·6	340·8
0·017	298	705·0	16·1	305·0	0·025	304·4	686·0	12·2	568·0
Heat of reaction 20·4 *kcal./mole*					*Heat of reaction* 7·3 *kcal/mole*				

* Vol. of NO absorbed per mole at N.T.P.
† Mean value of $(p_{NO}[FeCl_2])/[FeCl_2NO]$.
‡ Mean value of $(p_{NO}[CuCl_2])/[CuCl_2NO]$.

On decomposition of the nitric oxide complex, the cupric ion is regenerated. This fact, together with the infrared and magnetic data, indicates that the complex must be formulated as $[Cu^I(C_2H_5{\cdot}OH)_3NO]^{2+}$, where the number of solvate molecules is most likely three, by analogy with the cupric aquo-complex ion.[26]

EXPERIMENTAL

Preparations.—Compounds were made and purified according to the following references: $2FeSO_4{\cdot}NO,13H_2O$,[7] $[Fe(NH_3)_5NO]Cl_2SO_4$.[17] and $Na_2[Fe(CN)_5NO]$ [18] from $Na_3[Fe(CN)_5NH_3]$.[27]

The brown-ring compounds were made from aqueous ferrous solutions containing a 3% excess of sulphuric, hydrochloric, or perchloric acid. Nitric oxide was obtained from a sodium nitrite–ferrous sulphate generator and any nitrogen dioxide was removed with concentrated potassium hydroxide.

Iron tetranitrosyl was made by Manchot and Enk's method,[23] slightly modified as follows. Iron pentacarbonyl (1·5 g.) was placed in a 20-ml. stainless-steel bomb (Baskerville and Lindsay Ltd., Manchester) in nitrogen. Nitric oxide was introduced from a cylinder at about 100 atm. and the bomb was then closed and held at room temperature for 3 days. It was then cooled to −70° and the tetranitrosyl removed and centrifuged at −40° in sodium-dried ether. The product shows no infrared carbonyl frequencies; it consists of a fine mass of long, dark brown-black needles which decompose on standing even at 0° [Found: Fe, 33·08. Calc. for $Fe(NO)_4$: Fe, 31·75].

[23] Manchot and Enk, *Annalen*, 1929, **470**, 275.
[23] Hieber and Beck, *Z. Naturforsch.*, 1958, **13b**, 194.
[24] Kohlschutter and Kutscheroff, *Ber.*, 1904, **37**, 3044.
[25] Manchot, *Ber.*, 1914, **47**, 1601.
[26] O'Brien, "Chemistry of Co-ordination Compounds," J. C. Bailar (Editor), Reinhold, New York, 1956.
[27] Hofmann, *Z. anorg. Chem.*, 1896, **12**, 146.

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Physical Measurements.—The compounds were handled in a nitrogen atmosphere throughout. Magnetic measurements were made in sealed 5-ml. Gouy solution tubes at fields of 8000 gauss. Infrared measurements were made on a Perkin-Elmer Model 21 instrument with sodium chloride optics. Solids were examined as Nujol mulls and aqueous solutions as films between arsenic sulphide plates, which were made airtight with an O-ring of grease. The near infrared and visible spectra were taken on a Perkin-Elmer "Spectracord" double-beam recording spectrophotometer. Gas absorption was measured in a conventional Warburg-type apparatus.

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806. *The Conductivity of Silver Salts in Non-aqueous and Mixed Solvents. Part VII.*[1]

By V. S. GRIFFITHS, K. S. LAWRENCE, and M. L. PEARCE.

The conductivity of silver nitrate in benzonitrile and in benzonitrile solutions containing ethanol and of silver perchlorate in pure and binary mixtures of acetone, *cyclo*hexanone, and *iso*butyl alcohol is reported and discussed.

PREVIOUS investigations [1] have all been directed at the preferential solvation of silver ions in non-aqueous solvents and solvent mixtures, the nature of the complex ions so formed, and the effects of the solvation on the dissociation of the salt and the mobility of the cation. Wherever solvation has occurred to any reasonable extent it has increased the dissociation. This has been explained as being because (*a*) increase in the size of the ion favours the dissociation process, (*b*) complex-ion formation effectively removes the ions formed by dissociation, and (*c*) preferential solvation of silver ions by one component of a binary solvent mixture may alter the dielectric constant and viscosity in the immediate vicinity of an ion from the bulk value. Effects (*a*) and (*b*) are inseparable but by choosing solvents of closely similar dielectric constants effect (*c*) can largely be eliminated and hence some idea of its importance obtained.

The conductivity of silver nitrate in benzonitrile and benzonitrile–ethanol and of silver perchlorate in pure and binary mixtures of acetone, *cyclo*hexanone, and *iso*butyl alcohol has been studied. The results for the silver nitrate solutions have been compared with those for the same electrolyte in other solvents having similar dielectric constants, due to other workers. The results are shown in the Figures and the Table.

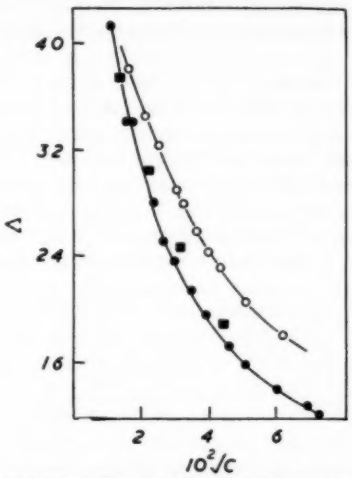
Solvent	Solute	$10^2\eta$ (P)	10^3K	Λ_0	a (Å)	$\Lambda_0\eta$	D
Ammonia (−33°) [a]	$AgNO_3$	0·26	4·85	291	3·38	0·756	22
Ethanol [b]	$AgNO_3$	1·09	4·40	44·8	2·72	0·489	24
90% Acetone–10% water [c]	$AgNO_3$	0·44	1·18	124	2·02	0·544	24
99% Benzonitrile–1% ethanol	$AgNO_3$	1·24	0·48	53·8	1·70	0·667	25
Benzonitrile	$AgNO_3$	1·24	0·25	55·2	1·58	0·684	25
Acetone [d]	$AgClO_4$	0·31	0·54	181	2·75	0·56	21
*cyclo*Hexanone	$AgClO_4$	2·2	0·88	27·5	2·99	0·60	18
*iso*Butyl alcohol	$AgClO_4$	4·3	1·47	12·2	3·42	0·53	18
22% Acetone–78% *cyclo*hexanone	$AgClO_4$	1·09	1·46	53·2	3·19	0·58	19
40% *iso*Butyl alcohol–60% *cyclo*hexanone	$AgClO_4$	2·55	0·95	21·2	3·05	0·54	18
55% Acetone–45% *iso*butyl alcohol	$AgClO_4$	0·68	2·18	81·4	3·20	0·55	20

[a] Franklin and Kraus, *Amer. Chem. J.*, 1900, **23**, 277. [b] Copely, Murray-Rust, and Hartley, *J.*, 1930, 2492. [c] Part III. [d] Part V.

Shedlovsky's extrapolation method [2] was used to determine the dissociation constants and values of Λ_0 from the experimental results and all plots were linear.

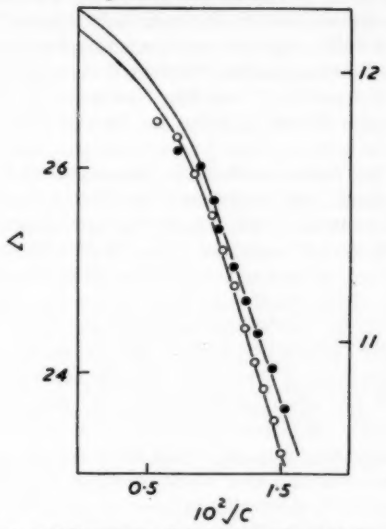
[1] Parts I—VI, *J.*, 1954, 686; 1955, 1208, 2797; 1956, 473; 1957, 3243; 1958, 309.
[2] Shedlovsky, *J. Franklin Inst.*, 1938, **225**, 739.

FIG. 1. *Equivalent conductances of silver nitrate solutions.*



● Benzonitrile. ○ 99% Benzonitrile–1% ethanol. ■ Martin's results for benzonitrile (ref. 3).

FIG. 2. *Equivalent conductances of silver perchlorate solutions.*



○ *cyclo*Hexanone (left-hand scale). ● *iso*-Butyl alcohol (right-hand scale).

FIG. 3. *Equivalent conductances of silver perchlorate in* 22% *acetone*–78% *cyclohexanone.*

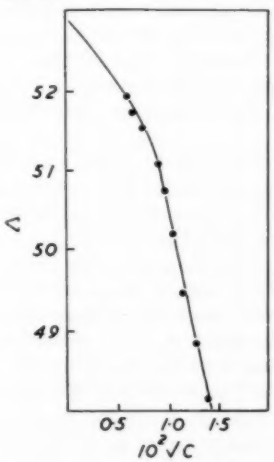
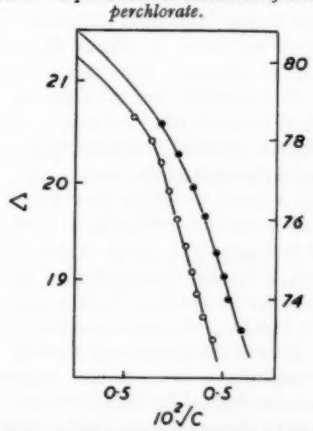


FIG. 4. *Equivalent conductances of silver perchlorate.*



○ 40% *iso*Butyl alcohol–60% *cyclo*hexane (left-hand scale). ● 55% Acetone–45% *iso*butyl alcohol (right-hand scale).

The behaviour of silver nitrate in benzonitrile has previously been studied by Martin [3] who obtained $\Lambda_0 = 52{\cdot}18$ by extrapolation. He also obtained a value for the dissociation constant of 4×10^{-4}, though more recently Davies [4] recalculated the value of Λ_0 as 50·20, thus altering the dissociation constant to $4{\cdot}72 \times 10^{-4}$. Fair agreement exists between the present results and Martin's, as shown by Fig. 1.

[3] Martin, *J.*, 1928, 3270.
[4] Davies, "Conductivity of Solutions," Chapman and Hall, London, 1933, p. 118.

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Fuoss and Kraus [5] pointed out that ammonia forms a stable complex with the silver ion and hence in this solvent the cation is relatively large and solvation, in the sense of solvent dipoles oriented by the ionic field, further increases the effective radius. They concluded that " silver nitrate was a much stronger electrolyte in ammonia of dielectric constant 22 than in benzonitrile of dielectric constant 25."

Ethanol is a " levelling " solvent (Part IV [1]), *i.e.*, one which solvates both the anion and cation. Hence, allowing for the retention of solvent molecules in the ion-pair and overlap of the solvent shells,[6] we are not surprised that the dissociation constant in this solvent is of the same order as in ammonia where only the cation is strongly solvated. Like ammonia, and in contrast to ethanol, benzonitrile is a " differentiating " solvent, and for silver nitrate it will solvate the cation preferentially, but its tendency to do so, compared with that of ammonia, is not likely to be so great, as the forces between solvent molecules and cations will be weaker than they are in ammonia, so that in benzonitrile association and electrolytic weakness will be favoured; the dissociation constant in benzonitrile, being the lowest in the Table, demonstrates this. However, benzonitrile and ethanol have very similar dielectric constants (25 and 24 respectively). Thus if preferential solvation by one component of a mixture of them should occur it is reasonable to assume that this would have less effect on the microscopic dielectric constant than if the two solvents had vastly different dielectric constants, as in the case of water and acetone. It has already been clearly demonstrated [1] that the value of the bulk dielectric constant is not the main factor in determining electrolyte strength—silver nitrate is a very weak electrolyte in acetone (Part II [1]), indicating little or no solvation of the ions in a solvent of dielectric constant of approximately 20—but the addition of a small quantity of organic base greatly increases the strength of the electrolyte whilst altering the dielectric constant of the solvent but little. This is not to say, however, that the increase in ionic size is the only factor influencing the dissociation constant, since the preferential absorption of the base will affect both the microscopic dielectric constant and viscosity, *i.e.*, the properties in the immediate vicinity of the ions. If any of the latter factors could be affected in any way the results would be of interest; although the use of ethanol and benzonitrile cannot eliminate the effects, it is possible that at least one of them could be reduced. The addition of 1% of ethanol to benzonitrile solutions of silver nitrate does increase the dissociation constant to some extent, probably mainly owing to solvation of the anion which increases the distance of closest approach of the ions.

With regard to silver perchlorate solutions the results indicate that a considerable degree of solvation, probably of both ionic species, exists in solutions containing *iso*butyl alcohol and also, to a small extent, those containing *cyclo*hexanone. It is difficult to see, however, why the dissociation is greater in acetone–alcohol than in the pure alcohol, though it is noteworthy that the values of the Bjerrum parameter for these two solutions are very similar. A possible explanation may be that the values of the dielectric constant for the solvent mixtures investigated, which were found by assuming a linear relationship with composition, are wrong. Indeed Osipov, Panina, and Lempert [7] showed that the dielectric isotherms for *iso*butyl alcohol–acetone mixtures were markedly curved. These values were obtained over a wide concentration range and no datum is available for small concentrations of either component, but on general grounds a sudden variation from linearity over the concentration range studied in the present paper is unlikely. Earlier papers [1] have described the technique of introducing deliberate errors into the computations in order to estimate their effect, and the variation in the dissociation constant seems unlikely to be explained on the assumption that the dielectric constant varies greatly.

The effects of solvation on the dissociation constant and distance of closest approach of the ions are qualitatively (Part VI [1]) and quantitatively similar to the effects of organic

[5] Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 1019.
[6] Grunwald, *Analyt. Chem.*, 1954, **26**, 1696.
[7] Osipov, Panina, and Lempert, *Zhur. obshchei Khim.*, 1953, **25**, 662.

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bases on the conductivity of the same salt in pure acetone, and since for the present investigations there are likely to be smaller variations of the dielectric constant in the vicinity of the ion than in the previous systems studied, it appears that variations in the dielectric constant play a relatively minor part in determining the dissociation constant. Hence the increase in the dissociation observed on the addition of a complex-forming solvent to a solution is due primarly to the inhibiting effect of the increase in ion size on the association process and/or possibly the formation of a new ionic species, rather than any variation in the dielectric constant near the ion.

On calculating the functions $\Lambda_0\eta$ and $V_0\eta/D$ for the solutions studied, we found that the latter is more constant as has also been observed by Ulich and Birr [8] for a variety of ions in solvents which do not extensively solvate them and by Rysselberghe and Frinstrom [9] for solutions of magnesium perchlorate in water, nitromethane, methyl alcohol and *iso*propyl alcohol; as yet no theoretical explanation has been found for this.

Experimental.—Procedure was as described in Part II.[1] "AnalaR" benzonitrile was distilled under reduced pressure, the middle fraction being dried ($CaCl_2$) and then repeatedly fractionated under reduced pressure in a stream of dry nitrogen until the specific conductivity was below $0{\cdot}04 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$. *cyclo*Hexanone and *iso*butyl alcohol was fractionated twice under reduced pressure in a stream of nitrogen. The purification of ethanol, acetone, and electrolytes was as described in Part I.[1]

The variation of viscosity with composition for binary mixtures of acetone, *cyclo*hexanone, and *iso*butyl alcohol was examined with an Ostwald viscometer.

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BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, February 14th*, 1958.]

[8] Ulich and Birr, *Z. angew. Chem.*, 1928, **41**, 443.
[9] Rysselberghe and Frinstrom, *J. Amer. Chem. Soc.*, 1945, **67**, 680.

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807. *The Preparation of 9α-Fluoro-analogues of Cortisol Acetate and Prednisolone Acetate from 11 : 20-Diketones of the 5α-Series.**

By J. ELKS, G. H. PHILLIPPS, and W. F. WALL.

3β : 17-Dihydroxy-5α-pregnane-11 : 20-dione and 3β-acetoxy-5α-pregn-16-ene-11 : 20-dione have been converted *via* 20-ethylene ketals into 3β : 11β : 17-trihydroxy-5α-pregnan-20-one. Dehydration to the $\Delta^{9:11}$-compound, acetoxylation at $C_{(21)}$, and oxidation gave 21-acetoxy-17-hydroxy-5α-pregn-9(11)-ene-3 : 20-dione. Formation of the 9β : 11β-epoxide and reaction with hydrogen fluoride then gave the 9α-fluoro-4 : 5α-dihydro-derivative of cortisol acetate, which was converted into the 9α-fluoro-analogues of cortisol acetate and of prednisolone acetate.

THE high glucocorticoid activity of the 9α-fluoro-analogues of cortisol (11β : 17 : 21-trihydroxypregn-4-ene-3 : 20-dione) [1] and prednisolone (11β : 17 : 21-trihydroxypregna-1 : 4-diene-3 : 20-dione) [1b, 2] led us to examine their preparation from compounds of the 5α-series,

* In this paper acceptance of recent I.U.P.A.C. recommendations is anticipated: the name 5α-pregnane is used in place of *allo*pregnane (see *J.*, 1951, 3527).

[1] (*a*) Fried and Sabo, *J. Amer. Chem. Soc.*, 1954, **76**, 1455; 1957, **79**, 1130; (*b*) Hirschmann, Miller, Wood, and Jones, *ibid.*, 1956, **78**, 4956.

[2] (*a*) Hirschmann, Miller, Beyler, Sarett, and Tishler, *ibid.*, 1955, **77**, 3166; (*b*) Fried, Florey, Sabo, Herz, Restivo, Borman, and Singer, *ibid.*, p. 4181; (*c*) Hogg, Lincoln, Nathan, Hanze, Schneider, Beal, and Korman, *ibid.*, p. 4438; (*d*) Vischer, Meystre, and Wettstein, *Helv. Chim. Acta*, 1955, **38**, 1502; (*e*) Meystre, Frey, Voser, and Wettstein, *ibid.*, 1956, **39**, 734.

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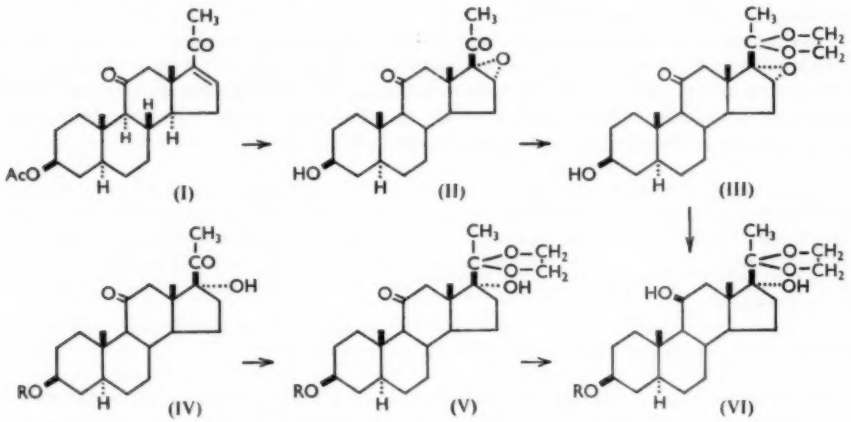
intermediate in the synthesis of cortisone from hecogenin. 3β : 17-Dihydroxy-5α-pregnane-11 : 20-dione [3] (IV; R = H) was a convenient starting material, since the formation from it of the 20-ketal [4] (V; R = H) was much more efficient than the ketalisation of 17 : 21-dihydroxy-20-oxo-steroids.[5] Reduction of the 20-ketal (V; R = H) with sodium borohydride gave an excellent yield of the 11β-alcohol (VI; R = H) with no significant quantity of the 11α-epimer.[5,6]

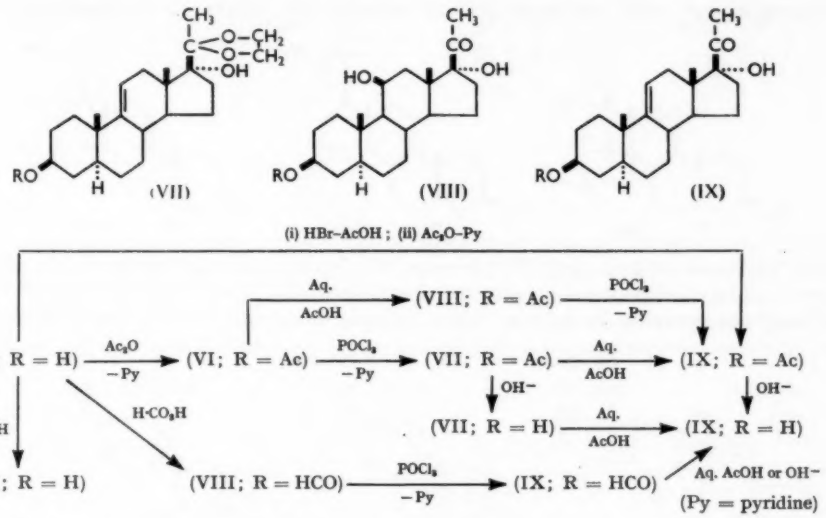


A shorter but lower-yielding route to the 11β-alcohol (VI; R = H) began with 3β-acetoxy-5α-pregn-16-ene-11 : 20 dione (I).[7] Reaction of this compound with alkaline hydrogen peroxide [3b] gave the 16α : 17-epoxide (II) which was in turn converted into its 20-ethylene ketal (III).[8] Reversal of the order of these reactions was not satisfactory, ketalisation of the 16-en-20-one [8] giving only a poor yield. Lithium aluminium hydride reduced both the 11-oxo- and the 16α : 17-epoxy-group of the 20-ketal (III) and gave the 11β : 17-diol (VI; R = H). Sodium borohydride, on the other hand, reduced only the 11-oxo-group, with formation of the 20-ethylene ketal of 16α : 17-epoxy-3β : 11β-dihydroxy-5α-pregnan-20 one.

Since an 11β-hydroxy-group may undergo oxidation [5c,9] or elimination [5c] during acid-catalysed bromination (such as is required at $C_{(21)}$ during some stage of the synthesis), the triol (VI; R = H) was next converted into the $\Delta^{9(11)}$-20-ketone (IX; R = H). Of the several routes examined, and shown in the chart (p. 4003), we preferred the one involving protection of the 3β-hydroxyl of (VI; R = H) as acetate, dehydration with phosphorus oxychloride in pyridine to the $\Delta^{9(11)}$-compound (VII; R = Ac), deketalisation with aqueous acetic acid to the 20-ketone (IX; R = Ac) and alkaline hydrolysis to the required 3β : 17-dihydroxy-5α-pregn-9(11)-en-20-one (IX; R = H). In the dehydration stage, low yields resulted from the use of pure dry reagents; however, addition of water [10] or phosphoric acid (but not of pyridine hydrochloride) allowed dehydration to proceed satisfactorily.

[3] (*a*) Barton, Evans, Hamlet, Jones, and Walker, *J.*, 1954, 747; (*b*) Pataki, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 5615.
[4] Djerassi, Batres, Romo, and Rosenkranz, *ibid.*, p. 3634; U.S.P. 2,702,291.
[5] (*a*) Antonucci, Bernstein, Heller, Lenhard, Littell, and Williams, *J. Org. Chem.*, 1953, **18**, 70; (*b*) Levin, Magerlein, McIntosh, Hanze, Fonken, Thompson, Searcy, Scheri, and Gutsell, *J. Amer. Chem. Soc.*, 1954, **76**, 546; (*c*) Evans, Green, Hunt, Long, Mooney, and Phillipps, *J.*, 1958, 1529.
[6] Oliveto, Clayton, and Hershberg, *J. Amer. Chem. Soc.*, 1953, **75**, 486; Magerlein and Levin, *ibid.*, p. 3654; Allen, Bernstein, and Littell, *ibid.*, 1954, **76**, 6116.
[7] Cameron, Evans, Hamlet, Hunt, Jones, and Long, *J.*, 1955, 2807.
[8] Cf. Bernstein, Heller, and Stolar, *J. Amer. Chem. Soc.*, 1954, **76**, 5674.
[9] Oliveto, Gerold, Weber, Jorgensen, Rausser, and Hershberg, *ibid.*, 1953, **75**, 5486.
[10] Graber, Haven, and Wendler, *ibid.*, p. 4722; Kemp, Kappas, Salamon, Herling, and Gallagher, *J. Biol. Chem.*, 1954, **210**, 123.

By avoiding purification of the intermediates, it was possible to obtain the pure $\Delta^{9(11)}$-compound (IX; R = Ac) in 74% yield from the 3β : 11β : 17-triol (VI; R = H).



The action of hydrogen bromide on the 3β : 11β : 17-triol (VI; R = H) caused elimination of the 11β-hydroxyl group [5c] and concurrent hydrolysis of the 20-ketal, but this route to the acetate (IX; R = Ac), although short, gave a low yield.

The product was identical with a sample prepared from hecogenin by a different route [11] and kindly supplied by Dr. R. K. Callow.

The 9 : 11-double bond of the 20-ketone (IX; R = H) did not seriously interfere with the bromination to the 21-bromo-20-ketone (X; R = H), provided this was done in chloroform containing alcohol and saturated with hydrochloric acid.[12] The crude bromo-compound with potassium acetate in acetone gave the 21-acetoxy-compound (XI; R = H), which was separated from unchanged 20-ketone (IX; R = H) and other reactive ketones by making use of its unreactivity to Girard reagent P.[13] Oxidation of the 3β-hydroxy-group of the monoacetate (XI; R = H) by chromic acid in acetone [14] gave 21-acetoxy-17-hydroxy-5α-pregn-9(11)-ene-3 : 20-dione (XII), identical with a specimen prepared from the 4 : 5α-dihydro-derivative of cortisone acetate.[5c]

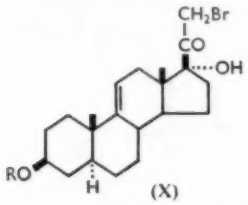
The 3β-hydroxy-20-ketone (IX; R = H) was very sparingly soluble in most solvents, and we examined the bromination and acetolysis of two of its more soluble derivatives. The 3-acetate (IX; R = Ac) was satisfactorily converted into the 3 : 21-diacetate (XI; R = Ac), but this was not taken further, since its conversion into the required 3-oxo-compound (XII) promised to be difficult. Bromination of the formate (IX; R = HCO) in methylene chloride containing ether, and subsequent addition of methanol to the acid solution, gave the 21-bromo-3β-alcohol (X; R = H), which was then converted into the 21-acetate (XI; R = H), but the overall yield was lower than that obtained by bromination of the 3β-hydroxy-compound (IX; R = H).

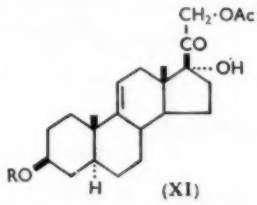
The introduction of a 4 : 5-double bond into $\Delta^{9(11)}$-3-ketones of the 5α-series is described elsewhere.[5c] We hoped that some of the difficulties of the reaction could be lessened if

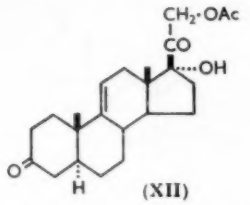
[11] Callow and James, *J.*, 1956, 4739.
[12] B.P. 761,009.
[13] B.P. 762,716; 757,803.
[14] Brooks, Hunt, Long, and Mooney, *J.*, 1957, 1175.

ring C contained a less reactive grouping than a double bond, and we therefore next investigated the conversion of the $\Delta^{9(11)}$-3-ketone (XII) into the fluorohydrin (XX).

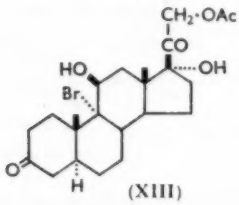
The 9 : 11-double bond of the compound (XII) reacted with *N*-bromoacetamide in aqueous dioxan, with perchloric acid as catalyst, but, unlike the bromohydrins from

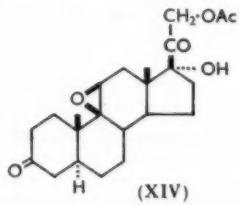

(X)

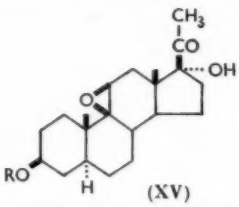

(XI)


(XII)

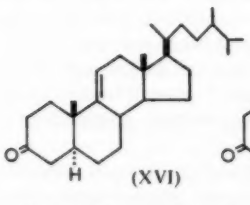
$\Delta^{4:9(11)}$-3-ketones [1a] and $\Delta^{1:4:9(11)}$-3-ketones [2b, 2c] described in the literature, the bromohydrin (XIII) lost bromine on attempted isolation. The crude products showed excess carbonyl absorption in the infrared region, possibly owing to formation of an 11-oxo-group

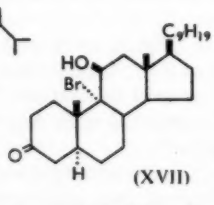

(XIII)

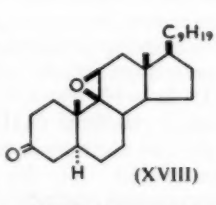

(XIV)

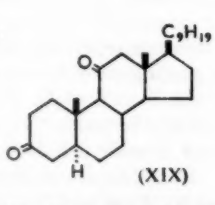

(XV)

(see below). The 9β : 11β-epoxide (XIV) was, however, obtained by ring closure of the unisolated bromohydrin with alkali and subsequent re-acetylation. Reaction of the epoxide with hydrogen bromide would be expected to regenerate the bromohydrin (XIII),[1a] but this product also was too unstable to be isolated. The bromohydrin derived from the simpler $\Delta^{9:11}$-compound (IX; R = H) was also found to be unstable (cf. ref. 11), but again the epoxide (XV; R = H) could be formed with alkali *in situ*.


(XVI)


(XVII)


(XVIII)

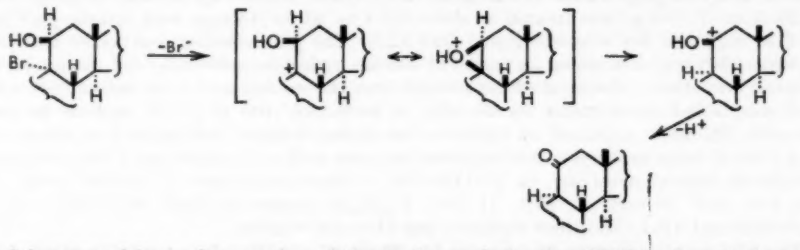

(XIX)

In model experiments ergost-9(11)-en-3-one (XVI) [5c] reacted with *N*-bromoacetamide to give crystallisable 9α-bromo-11β-hydroxyergostan-3-one [15] (XVII), which on treatment with potassium acetate in boiling ethanol [1] or when boiled in ethanol alone yielded mixtures of the 9β : 11β-epoxide (XVIII) and ergostane-3 : 11-dione (XIX). The formation of the latter compound recalls the acid isomerisation in the cholanic acid series of a 9α : 11β-diol to the corresponding 11-ketone; [16] the unusual *cis*-elimination was attributed to the intermediate formation of a 9-carbonium ion; a similar mechanism may operate in the formation of our ketone (XIX).

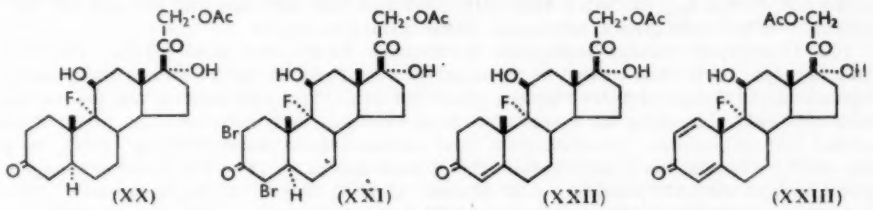
Ring closure of the bromohydrin (XVII) to the 9β : 11β-epoxide (XVIII) was achieved in good yield by the use of potassium *tert.*-butoxide in *tert.*-butyl alcohol at room temperature.[15]

[15] Cf. Henbest, Jones, Wagland, and Wrigley, *J.*, 1955, 2477.
[16] Heyman and Fieser, *J. Amer. Chem. Soc.*, 1951, **73**, 5252.

Reaction of the 9β : 11β-epoxide (XIV) with hydrogen fluoride in chloroform [1] gave the 9α-fluoro-11β-alcohol (XX), whose physical properties agreed with those reported [2a, b] for



material prepared by hydrogenation of the 9α-fluoro-derivative (XXII) of cortisol acetate. Dibromination in acetic acid and acid-catalysed rearrangement then gave the crude 2 : 4-dibromo-3-ketone (XXI), which was used without purification. Treatment with sodium iodide in acetone containing bromoacetone [17] and subsequent deiodination with chromous chloride gave a crude product containing both the saturated 3-ketone (XX) and



the Δ^4-3-ketone (XXII). Separation with Girard reagent P and chromatography gave a low yield of the 9α-fluoro-derivative (XXII) of cortisol acetate.

The crude dibromo-3-ketone (XXI) was also dehydrobrominated by means of semicarbazide, as described elsewhere for an analogue.[18] Separation with Girard reagent P [19] and chromatography of the unreactive ketones gave a very low yield of the 9α-fluoro-derivative (XXIII) of prednisolone acetate which was identified by infrared spectroscopy and, as expected, had powerful liver glycogen activity.

Experimental

Rotations were determined on *ca.* 1% solutions in $CHCl_3$, and ultraviolet spectra in ethanol, unless otherwise stated. M. p.s were taken on a Kofler block. A Perkin–Elmer model 21 double-beam spectrophotometer equipped with rock-salt optics was used for the determination of infrared spectra.

3β : 17-*Dihydroxy-5α-pregnane*-11 : 20-*dione* 20-*Ethylene Ketal* (V; R = H).—3β : 17-Dihydroxy-5α-pregnane-11 : 20-dione (IV; R = H) (20 g.) and toluene-*p*-sulphonic acid (0·3 g.) were refluxed for 2½ hr. (air condenser) in dry ethylene glycol (1 l.) at 100°/20 mm., with a nitrogen leak. The steroid dissolved in about 20 min. and the ketal then began to crystallise. The cooled suspension was poured into water (*ca.* 10 l.) containing an excess of sodium hydrogen carbonate, and after 1 hr. the precipitate was collected, washed with water, and dried at 90°/20 mm. The product (21·48 g., 95·5%) had m. p. 252—255°, $[\alpha]_D$ +31°, and on crystallisation from aqueous methanol containing a drop of pyridine it gave the 20-*ketal*, m. p. 254—257°, $[\alpha]_D$ +30·6° (Found: C, 70·5; H, 9·0. $C_{23}H_{36}O_5$ requires C, 70·4; H, 9·2%), $\nu_{max.}$ (in Nujol) 3450 (OH), 1692 (ketone), and 1082 and 1044 cm.$^{-1}$ (ketal).

The diol was acetylated with pyridine and acetic anhydride overnight at room temperature. The 3-*monoacetate* (V; R = Ac) separated from methanol with a drop of pyridine as needles,

[17] Evans, Hamlet, Hunt, Jones, Long, Oughton, Stephenson, Walker, and Wilson, *J.*, 1956, 4356.
[18] B.P. 788,306.
[19] B.P. 788,307.

m. p. 197—199°, $[\alpha]_D$ +17° (Found: C, 69·1; H, 8·8. $C_{25}H_{38}O_6$ requires C, 69·1; H, 8·8%), $\nu_{max.}$ (in CS_2) 3620 (OH), 1734 and 1240 (OAc), 1706 (ketone), and 1080 and 1044 cm.$^{-1}$ (ketal).

3β-*Hydroxy*-5α-*pregn*-16-*ene*-11 : 20-*dione* 20-*Ethylene Ketal*.—3β-Acetoxy-5α-pregn-16-ene-11 : 20-dione (I) (5·0 g.) was treated as above for 4 hr. at 95°/15 mm. with toluene-*p*-sulphonic acid (150 mg.) and dry ethylene glycol (125 ml.). The pink solution was cooled and poured into water (800 ml.) containing an excess of sodium hydrogen carbonate, and the product was extracted into ether. Removal of the solvent from the washed and dried extract left a froth, which was boiled under reflux for 30 min. in methanol (100 ml.) and aqueous 2N-sodium hydroxide (25 ml.). Addition of water to the cooled solution precipitated a gummy solid (3·3 g.) which, after two crystallisations from aqueous methanol containing a drop of pyridine, gave the 20-*ketal* as a solvate, m. p. 112—115°. After desolvation at 110°/0·1 mm. it had m. p. 150—155° (Found: C, 73·9; H, 9·0. $C_{23}H_{34}O_4$ requires C, 73·8; H, 9·15%), $\nu_{max.}$ (in Nujol) 3550 and 3300 (OH), 1698 (ketone), and 1190 cm.$^{-1}$ (ketal).

16α : 17-*Epoxy*-3β-*hydroxy*-5α-*pregnane*-11 : 20-*dione* (II).—3β-Acetoxy-5α-pregn-16-ene-11 : 20-dione (I) (1·0 g.) in methanol (50 ml.) was treated at room temperature with aqueous 4N-sodium hydroxide (2·0 ml.) and hydrogen peroxide (100-vol.; 4·0 ml.) and then kept at 0—5° for 16 hr. Dilution of the suspension with water and filtration gave a crystalline product (0·76 g.), m. p. 170—173° which, on recrystallisation from aqueous methanol, yielded the *epoxide* as plates, m. p. 173—175°, $[\alpha]_D$ +90° (Found: C, 72·7; H, 8·3. $C_{21}H_{30}O_4$ requires C, 72·8; H, 8·7%), $\nu_{max.}$ (in Nujol) 3520 (OH), 1708 and 1695 (ketones), and 994 and 852 cm.$^{-1}$ (epoxide): it had only general absorption in the ultraviolet region.

16α : 17-*Epoxy*-3β-*hydroxy*-5α-*pregnane*-11 : 20-*dione* 20-*Ethylene Ketal* (III).—The foregoing epoxide (1·0 g.) was treated in the usual way for 2½ hr. at 95°/13 mm. with toluene-*p*-sulphonic acid (20 mg.) and dry ethylene glycol (50 ml.). The pink solution was poured into water (300 ml.) containing an excess of sodium hydrogen carbonate, and the product was isolated with chloroform. Crystallisation from methanol gave plates (480 mg., 43%), m. p. 164—167°. After further crystallisation, the 20-*ketal* had m. p. 177—179° (after a change of crystal form at 170—173°) and $[\alpha]_D$ +67° (Found: C, 70·9; H, 8·8. $C_{23}H_{34}O_5$ requires C, 70·7; H, 8·8%), $\nu_{max.}$ (in Nujol) 1704 (ketone) and 1194 cm.$^{-1}$ (ketal).

16α : 17-*Epoxy*-3β : 11β-*dihydroxy*-5α-*pregnan*-20-*one* 20-*Ethylene Ketal*.—16α : 17-Epoxy-3β-hydroxy-5α-pregnane-11 : 20-dione 20-ethylene ketal (100 mg.) and sodium borohydride (100 mg.) were boiled together under reflux for 3 hr. in ethanol (10 ml.) and water (2 ml.). The solution was diluted with water and concentrated *in vacuo* to yield crystals (95 mg.), m. p. 168—172°. Further crystallisation from aqueous methanol gave 16α : 17-*epoxy*-3β : 11β-*dihydroxy*-5α-*pregnan*-20-*one* 20-*ethylene ketal* as needles, m. p. 169·5—173°, $[\alpha]_D$ +43° (Found: C, 70·2; H, 9·1. $C_{23}H_{36}O_5$ requires C, 70·4; H, 9·2%), $\nu_{max.}$ (in Nujol) 3500 (OH) and 1180 cm.$^{-1}$ (ketal).

3β : 11β : 17-*Trihydroxy*-5α-*pregnan*-20-*one* 20-*Ethylene Ketal* (VI; R = H).—(a) *From* 3β : 17-*dihydroxy*-5α-*pregnane*-11 : 20-*dione* 20-*ethylene ketal* (V; R = H). The 11-ketone (21·25 g.) and sodium borohydride (5·3 g.) were boiled under reflux for 2 hr. in ethanol (320 ml.) and water (32 ml.). The solution was diluted with water (160 ml.) and concentrated, finally *in vacuo*, to give a suspension of the crystalline product (21·25 g., 99·7%), m. p. 191—194°, $[\alpha]_D$ +7·3°, which was filtered off after addition of more water. Crystallisation from aqueous methanol containing a drop of pyridine gave the *triol* as glistening plates of a solvate, m. p. 150° then 192—196°, which, after desolvation, had only the higher m. p. and $[\alpha]_D$ +8° (Found: C, 69·7; H, 9·6. $C_{23}H_{38}O_5$ requires C, 70·0; H, 9·7%), $\nu_{max.}$ (in Nujol) 3600—3400 (OH) and 1076 and 1040 cm.$^{-1}$ (ketal). On one occasion material of the same m. p. was obtained, which differed from the usual material in its infrared spectrum in Nujol, but not in chloroform.

Acetylation of the triol with acetic anhydride and pyridine at room temperature and crystallisation from methanol gave the 3-*monoacetate* (VI; R = Ac) as prisms, m. p. 242—245°, $[\alpha]_D$ +1·3° (Found: C, 68·5; H, 9·25. $C_{25}H_{40}O_6$ requires C, 68·8; H, 9·25%), $\nu_{max.}$ (in Nujol) 3600 and 3480 (OH), 1722 and 1245 (OAc), and 1080 and 1042 cm.$^{-1}$ (ketal).

Hydrolysis of the 3-monoacetate with potassium hydrogen carbonate in boiling aqueous methanol regenerated the triol (VI; R = H).

(b) *From* 16α : 17-*epoxy*-3β-*hydroxy*-5α-*pregnane*-11 : 20-*dione* 20-*ethylene ketal* (III). The epoxide (100 mg.) in dry tetrahydrofuran (20 ml.) was treated with lithium aluminium hydride in ether (6·5% solution; 5 ml.), and the mixture was then boiled under reflux for 5 hr. The excess of reagent was destroyed by addition of ethyl acetate, and the suspension was diluted

with ether (80 ml.) and shaken with dilute sodium hydroxide solution. The ether layer was washed twice with water, dried, and evaporated to dryness. The residue crystallised from aqueous methanol, to give the triol (VI; R = H) as plates (68 mg., 67%), m. p. 189—194°, $[\alpha]_D$ +8°.

3β-*Acetoxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* 20-*Ethylene Ketal* (VII; R = Ac).—3β-Acetoxy-11β : 17-dihydroxy-5α-pregnan-20-one 20-ethylene ketal (3·0 g.) in dry pyridine (24 ml.) was added at room temperature to a mixture of phosphoric acid (0·5 ml.) and phosphorus oxychloride (6 ml.) in pyridine (24 ml.). After 24 hr. the suspension was poured into ice and water (500 ml.). The precipitated product (2·84 g., 100%), m. p. 198—203°, $[\alpha]_D$ −9°, was crystallised from methanol to give the $\Delta^{9(11)}$-*compound* as plates, m. p. 201—203°, $[\alpha]_D$ −8·8° (Found: C, 71·6; H, 9·1. $C_{25}H_{38}O_5$ requires C, 71·7; H, 9·1%), $\nu_{max.}$ (in CS_2) 3620 (OH), 1733 and 1240 (OAc), and 1092 cm.$^{-1}$ (ketal).

Treatment of the acetate with boiling methanolic sodium hydroxide for 1 hr. and crystallisation from methanol gave hexagonal plates of 3β : 17-*dihydroxy*-5α-*pregn*-9(11)-*en*-20-*one* 20-*ethylene ketal* (VII; R = H) as a methanol solvate, m. p. 224—227°, $[\alpha]_D$ −8° (Found: C, 70·6; H, 9·7. $C_{23}H_{36}O_4$,CH_3·OH requires C, 70·6; H, 9·9%), $\nu_{max.}$ (in Nujol) 3550 and 3350 (OH), 1092 (ketal), and 1645 and 812 cm.$^{-1}$ (trisubstituted ethylene).

3β-*Acetoxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (IX; R = Ac).—(a) *From* 3β-*acetoxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* 20-*ethylene ketal* (VII; R = Ac). The ketal (2·63 g.) was heated at 100° for 30 min. in 50% aqueous acetic acid (150 ml.). Addition of water to the cooled solution gave a precipitate (2·36 g.), m. p. 195—199°, $[\alpha]_D$ −12°, which, on crystallisation from methanol, gave the 20-ketone (IX; R = Ac), m. p. 202—205°, $[\alpha]_D$ −14° (Found: C, 74·1; H, 9·2. Calc. for $C_{23}H_{34}O_4$: C, 73·8; H, 9·15%), $\nu_{max.}$ (in Nujol) 3470 (OH), 1712 and 1258 (OAc), 1712 (ketone), 1350 ($COCH_3$), and 818 cm.$^{-1}$ (trisubstituted ethylene). Callow and James [11] give m. p. 198·5—200·5°, $[\alpha]_D$ −15°; a mixed m. p. with a sample kindly supplied by Dr. R. K. Callow was undepressed.

(b) *From* 3β : 11β : 17-*trihydroxy*-5α-*pregnan*-20-*one* 20-*ethylene ketal* (VI; R = H). The triol (10·85 g.) in glacial acetic acid (310 ml.) was treated with 5·5N-hydrogen bromide in acetic acid (30 ml.). The optical rotation of the solution rose rapidly during the first minute, and then began to fall at about the same rate. The rate of change of rotation had become slow and steady after 30 min. and the yellow solution was then poured into water (3 l.), and the product isolated with methylene chloride. Treatment of the residue with aqueous-methanolic sodium hydroxide gave crude 3β : 17-dihydroxy-5α-pregn-9(11)-en-20-one (IX; R = H), which could not readily be purified by crystallisation. With acetic anhydride in pyridine and crystallisation it gave the 3-monoacetate (IX; R = Ac) (35%), m. p. 197—201° (from methanol), $[\alpha]_D$ −10·3°.

(c) *From* 3β-*acetoxy*-11β : 17-*dihydroxy*-5α-*pregnan*-20-*one* (VIII; R = Ac). The 11β : 17-diol (see below) (500 mg.) in dry pyridine (4 ml.) was added to a solution of phosphorus oxychloride (0·3 ml.) in pyridine (4 ml.) and after 22 hr. at room temperature the suspension was poured into ice and water (150 ml.). The precipitated product, on crystallisation from methanol, gave the $\Delta^{9:11}$-compound (IX; R = Ac) (280 mg., 59%), m. p. 201·5—204°, $[\alpha]_D$ −14°.

3β : 17-*Dihydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (IX; R = H).—(a) *From* 3β-*acetoxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (IX; R = Ac). The 3-acetate (136 g.) and potassium hydrogen carbonate (45·2 g.) were boiled under reflux for 2½ hr. in methanol (4500 ml.) and water (1120 ml.). The acetate gradually dissolved during the first hour, and the product then began to separate. Most of the solvent was removed *in vacuo*, and water was added to precipitate the product (118·5 g., 98·5%), m. p. 235—240°, $[\alpha]_D$ −18°. Crystallisation from methanol gave the *diol* with m. p. 236—242°, $[\alpha]_D$ −15° (*c* 0·35) (Found: C, 76·0; H, 9·6. $C_{21}H_{32}O_3$ requires C, 75·9; H, 9·7%), $\nu_{max.}$ (in Nujol) 3550 and 3350 (OH), 1692 (ketone), 1350 ($CO{\cdot}CH_3$), and 820 cm.$^{-1}$ (trisubstituted ethylene).

The diol with acetic anhydride and pyridine re-formed the 3-monoacetate, m. p. 198—202°, $[\alpha]_D$ −14°.

(b) *From* 3β : 17-*dihydroxy*-5α-*pregn*-9(11)-*en*-20-*one* 20-*ethylene ketal* (VII; R = H). The methanol solvate (200 mg.) of the ketal was heated at 100° for 30 min. in acetic acid (8 ml.) and water (4 ml.). Water (100 ml.) was added to the cooled solution and the crystalline 20-ketone (IX; R = H) (167 mg., 100%), m. p. 235—240°, $[\alpha]_D$ −16° (*c* 0·3), was collected by filtration.

(c) *From* 3β-*formyloxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (IX; R = HCO). The formate

XUM

(see below) (500 mg.) was heated at 100° for 40 min. in acetic acid (20 ml.) and water (10 ml.). Isolation of the product as in (b) gave the 3β-hydroxy-compound (IX; R = H) (440 mg., 96%), m. p. 228—236°, $[\alpha]_D$ −15° (*c* 0·35).

3β : 11β : 17-*Trihydroxy-5α-pregnan*-20-*one* (VIII; R = H).—3β : 11β : 17-Trihydroxy-5α-pregnan-20-one 20-ethylene ketal (VI; R = H) (500 mg.) was heated at 100° for 30 min. in 50% aqueous acetic acid (20 ml.). Addition of water to the resultant suspension gave crystals (410 mg., 92·5%), m. p. 255° then 270—275°, $[\alpha]_D$ +32° (*c* 0·43 in AcOH), which, on recrystallisation from aqueous methanol, yielded the 20-*ketone* as elongated prisms, m. p. 260° and, after resolidification, 290° (decomp.), $[\alpha]_D$ +31° (*c* 0·35 in AcOH) (Found: C, 71·55; H, 9·5. $C_{21}H_{34}O_4$ requires C, 71·95; H, 9·8%), $\nu_{max.}$ (in Nujol) 3400 (OH), 1690 (ketone), and 1350 cm.$^{-1}$ ($CO{\cdot}CH_3$).

3β-*Acetoxy*-11β : 17-*dihydroxy-5α-pregnan*-20-*one* (VIII; R = Ac) *from* 3β-*Acetoxy*-11β : 17-*dihydroxy-5α-pregnan*-20-*one* 20-*Ethylene Ketal* (VI; R = Ac).—(a) *With aqueous acetic acid.* The 20-ketal (1·25 g.) was heated at 100° for 30 min. in 50% aqueous acetic acid (60 ml.), and water was added. The crystalline product (1·03 g., 90%), m. p. 209—213°, $[\alpha]_D$ +8°, was recrystallised from aqueous methanol. The 20-*ketone* first separated as small plates, which changed to prisms in one day. The two crystalline forms both had m. p. 213—216°, $[\alpha]_D$ +8° (Found: C, 70·5; H, 9·2. $C_{23}H_{36}O_5$ requires C, 70·4; H, 9·2%), but differed in their infrared spectra in Nujol. The plates showed $\nu_{max.}$ 3530 (OH), 1730 and 1250 (OAc), 1694 (ketone), and 1352 cm.$^{-1}$ ($CO{\cdot}CH_3$) whereas the prisms showed $\nu_{max.}$ 3500 (OH), 1710 and 1273 weak, 1732 and 1248 (OAc), 1700 (ketone), and 1352 cm.$^{-1}$ ($CO{\cdot}CH_3$). The two forms had identical spectra in bromoform, confirming their polymorphism.[20]

(b) *With formic acid in benzene.* The 20-ketal (5·0 g.) was boiled in benzene (250 ml.) and 98% formic acid (50 ml.) with distillation of 200 ml. in 2 hr. More benzene (200 ml.) was then added, and distilled during 1 hr. Removal of the remaining solvent *in vacuo* left crystals (4·4 g., 98%), m. p. 195—209°, which, on crystallisation from aqueous methanol, gave the 20-ketone (3·5 g., 78%), m. p. 210—213°, $[\alpha]_D$ +8°.

3β-*Formyloxy*-11β : 17-*dihydroxy-5α-pregnan*-20-*one* (VIII; R = HCO).—3β : 11β : 17-Trihydroxy-5α-pregnan-20-one 20-ethylene ketal (VI; R = H) (15 g.) in benzene (150 ml.) and 98% formic acid (37·5 ml.) were concentrated to 60 ml. during 2 hr. Benzene (120 ml.) was added, and after concentration to 40 ml. and dilution with light petroleum (400 ml.) the product (13·3 g., 97%) separated as crystals, m. p. 169—175°, $[\alpha]_D$ 0°. Crystallisation from benzene gave the *formate* with m. p. 184—186°, $[\alpha]_D$ −2° (Found: C, 70·0; H, 8·8. $C_{22}H_{34}O_5$ requires C, 69·8; H, 9·0%), $\nu_{max.}$ (in Nujol) 3550 and 3450 (OH), 1680 (ketone), and 1704 and 1175 cm.$^{-1}$ (formate).

3β-*Formyloxy*-17-*hydroxy-5α-pregn*-9(11)-*en*-20-*one* (IX; R = HCO).—(a) *From* 3β : 17-*dihydroxy-5α-pregn*-9(11)-*en*-20-*one* (IX; R = H). The diol (5·0 g.) in benzene (250 ml.) was treated as above with 98% formic acid (50 ml.). The product separated from benzene as crystals (3·95 g., 73%), m. p. 183—186°, $[\alpha]_D$ −15·5°. A second crop (0·7 g., 13%), m. p. 178—180°, $[\alpha]_D$ −18°, was obtained by addition of light petroleum to the mother-liquors. Recrystallisation from *cyclo*hexane gave the *formate* with m. p. 185—189°, $[\alpha]_D$ −16° (Found: C, 73·5; H, 9·0. $C_{22}H_{32}O_4$ requires C, 73·3; H, 9·0%), $\nu_{max.}$ (in Nujol) 3500 (OH), 1695 (ketone), 1695 and 1216 (formate), 1350 ($CO{\cdot}CH_3$), and 818 cm.$^{-1}$ (trisubstituted ethylene).

(b) *From* 3β-*formyloxy*-11β : 17-*dihydroxy-5α-pregnan*-20-*one* (VIII; R = HCO). The diol was dehydrated with phosphorus oxychloride and phosphoric acid in pyridine, as described for the acetate (VIII; R = Ac). Crystallisation of the crude product from benzene–light petroleum (1 : 1) gave the $\Delta^{9:11}$-compound (59%), m. p. 184—186°, $[\alpha]_D$ −17°.

21-*Acetoxy*-3β : 17-*dihydroxy-5α-pregn*-9(11)-*en*-20-*one* (XI; R = H).—(a) *From* 3β : 17-*dihydroxy-5α-pregn*-9(11)-*en*-20-*one* (IX; R = H). A vigorously stirred suspension of the finely divided 20-ketone (90 g.) in chloroform (1800 ml.) containing 1% of alcohol was saturated with hydrogen chloride during 15 min., and a solution of bromine (15·0 ml.) in chloroform (500 ml.) was then added during 45 min. After a further 5 min. ether (4500 ml.) was added and after 25 min. the solid was filtered off. The filtrate was washed with water, aqueous sodium hydrogen carbonate, and water, dried, and evaporated to dryness *in vacuo*. The residual pale yellow gum was combined with filtered solid and boiled under reflux for 2 hr., with stirring, in acetone (5 l.) containing anhydrous potassium acetate (270 g.).

Removal of the acetone *in vacuo* and addition of water precipitated the crude product

[20] Dickson, Page, and Rogers, *J.*, 1955, 443.

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(109 g.), which was boiled under reflux for 45 min. with Girard reagent P (51 g.) in dry methanol (2250 ml.) and acetic acid (112 ml.). The suspension was cooled to 5°, and after 18 hr. the crystalline product (76·7 g., 73%) was collected, washed with cold methanol, and dried at 90°/20 mm.; it had m. p. 235—238°, $[\alpha]_D$ +45° (*c* 0·4), and showed $\nu_{max.}$ (in Nujol) 3600—3500 (OH) and 1720 and 1240 cm.$^{-1}$ (OAc). Crystallisation from methanol gave 21-*acetoxy*-3β : 17-*dihydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (XI; R = H) as a methanol solvate, m. p. 239—241°, $[\alpha]_D$ +42° (*c* 0·53). Its infrared spectrum showed $\nu_{max.}$ (in Nujol) 3600 and 3450 (OH), 1760 and 1210 (OAc), and 1724 cm.$^{-1}$ (ketone), and differed from that of the unsolvated crude material. For analysis it was desolvated at 120°/0·1 mm. (Found: C, 71·0; H, 9·0. $C_{23}H_{34}O_5$ requires C, 70·7; H, 8·8%).

The mother-liquors from the Girard purification were poured into water containing an excess of sodium hydrogen carbonate, and the rest of the unreactive material was isolated with ether as a yellow glass (11·6 g.) which did not crystallise satisfactorily. The aqueous phase from the extraction was acidified with hydrochloric acid and extracted with ether. The residue was acetylated and crystallised, to give 3β-acetoxy-17-hydroxy-5α-pregn-9(11)-en-20-one (3·5%), m. p. 199—201°, $[\alpha]_D$ −12°.

Acetylation of the 21-acetate (XI; R = H) with acetic anhydride and pyridine, and crystallisation from ethyl acetate gave the 3 : 21-diacetate (XI; R = Ac) as plates, m. p. 227—230°, $[\alpha]_D$ +40°, after drying at 100°/10 mm., identical with material prepared from 3β-acetoxy-17-hydroxy-5α-pregn-9(11)-en-20-one (IX; R = Ac) as described below.

(b) *From* 3β-*formyloxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (IX; R = HCO). A solution of the formate (3·0 g.) in methylene chloride (40 ml.) and ether (10 ml.) was saturated with hydrogen chloride and then brominated as described in (a). Methanol (5 ml.) was then added, and the crude bromo-compound isolated, treated with potassium acetate, and purified as in (*a*), to give the 21-acetate (XI; R = H) (1·45 g., 45%), m. p. 232—235°, $[\alpha]_D$ +42° (*c* 0·3).

3β : 21-*Diacetoxy*-17-*hydroxy*-5α-*pregn*-9(11)-*en*-20-*one* (XI; R = Ac).—A solution of 3β-acetoxy-17-hydroxy-5α-pregn-9(11)-en-20-one (IX; R = Ac) (3·0 g.) in chloroform containing 1% of alcohol (45 ml.) was saturated with hydrogen chloride during 10 min. and a solution of bromine (1·35 g., 1·05 mol.) in chloroform (15 ml.) was then added dropwise to the stirred solution during 15 min. After a further 5 min. the pale yellow solution was washed with water, aqueous sodium hydrogen carbonate, and water, and the solvent was removed *in vacuo* from the dried solution. The crude 21-bromo-compound (4·0 g.) was treated with potassium acetate and Girard reagent as described above for the 3β-hydroxy-compound, to give the 3 : 21-*diacetate* (2·55 g., 72%), m. p. 221—225°. Further crystallisation from ethyl acetate and drying at 100°/10 mm. gave material with m. p. 225—229° and $[\alpha]_D$ +41° (Found: C, 69·2; H, 8·2. $C_{25}H_{36}O_6$ requires C, 69·4; H, 8·4%), $\nu_{max.}$ (in Nujol) 3500 (OH), 1745 and 1238 (21-OAc), 1730 (20-ketone), 1704 (ketone), and 1704 and 1262 cm.$^{-1}$ (OAc).

21-*Acetoxy*-17-*hydroxy*-5α-*pregn*-9(11)-*ene*-3 : 20-*dione* (XII).—N-Potassium dichromate in 3N-sulphuric acid (180 ml.) was added to a boiling solution of 21-acetoxy-3β : 17-dihydroxy-5α-pregn-9(11)-en-20-one (XI; R = H) (15 g.) in acetone (4500 ml.), and after 5 min. most of the acetone was removed by distillation *in vacuo*. Precipitation with water, crystallisation from ethyl acetate, and drying for 24 hr. at 100°/10 mm. gave the 3-ketone as plates (12·6 g., 84·5%), m. p. 247—249°, $[\alpha]_D$ +66° (*c* 0·3). A further 6% was obtained by oxidation of material from the mother-liquors.

The compound was identical with material prepared from 4 : 5α-dihydrocortisone acetate *via* the bis-ketal.[5c]

The finely divided 21-acetate (600 mg.) was shaken for 4 days at room temperature in suspension in 1·8% aqueous sodium hydroxide (4·5 ml.) and dioxan (17 ml.). The crystalline product (530 mg.), m. p. 235—245°, was filtered off after addition of much water, and recrystallised from aqueous dioxan to give, after drying at 120°/0·1 mm., 17 : 21-*dihydroxy*-5α-*pregn*-9(11)-*ene*-3 : 20-*dione*, m. p. 235—240°, $[\alpha]_D$ +55° (*c* 0·42 in dioxan) (Found: C, 73·0; H, 9·0. $C_{21}H_{30}O_4$ requires C, 72·8; H, 8·7%), $\nu_{max.}$ (in Nujol) 3550—3500 (OH), 1702 (ketone), and 814 cm.$^{-1}$ (trisubstituted ethylene).

21-*Acetoxy*-9β : 11β-*epoxy*-17-*hydroxy*-5α-*pregnane*-3 : 20-*dione* (XIV).—A hot solution of 21-acetoxy-17-hydroxy-5α-pregn-9(11)-ene-3 : 20-dione (12·12 g.) in pure dioxan (3640 ml.) and water (485 ml.) was cooled quickly to 30° under nitrogen whereupon the steroid started to separate. *N*-Bromoacetamide (12·12 g.) and then 3% aqueous perchloric acid (242 ml.) were added immediately. In 15 min. the steroid redissolved, and after a further 10 min. the excess of

N-bromoacetamide was destroyed by addition of aqueous sodium pyrosulphite until the yellow colour disappeared. Aqueous 2N-sodium hydroxide (460 ml.) was added, together with sufficient water (900 ml.) to give a single phase, and after 20 min. the pale brown solution was acidified with acetic acid (60 ml.). The dioxan was distilled from the almost decolorised solution *in vacuo*, and the aqueous residue was diluted with water and extracted with chloroform. Removal of the solvent *in vacuo* left a solid (11 g.), which was treated with acetic anhydride and pyridine at 100°. Crystallisation of the product from ethyl acetate gave the *epoxide* (6·83 g., 54·5%), m. p. 201—206°, $[\alpha]_D$ +67°. Further crystallisation gave material with m. p. 205—208° and $[\alpha]_D$ +69° (Found: C, 68·4; H, 8·2. $C_{23}H_{32}O_6$ requires C, 68·3; H, 8·0%), $\nu_{max.}$ (in Nujol) 3550 (OH), 1752 and 1224 (21-OAc), and 1720 cm.$^{-1}$ (ketone), $\nu_{max.}$ (in $CHBr_3$) 1742 and 1230 (21-OAc), 1725 (20-ketone), and 1708 cm.$^{-1}$ (ketone).

21-*Acetoxy*-9α-*fluoro*-11β : 17-*dihydroxy*-5α-*pregnane*-3 : 20-*dione* (XX).—Anhydrous hydrogen fluoride (4·0 ml.) was added at 0° to a solution of 21-acetoxy-9β : 11β-epoxy-17-hydroxy-5α-pregnane-3 : 20-dione (XIV) (3·0 g.) in dry chloroform (300 ml.). During 4 hr. at 0°, with occasional swirling, the chloroform solution became pale brown and the supernatant hydrogen fluoride dark purple. The mixture was poured into aqueous sodium hydrogen carbonate, and the pale yellow chloroform layer was washed twice with water, dried, and evaporated. The residual froth was triturated with methanol and, after separation of an unidentified by-product (100 mg.), the solvent was removed *in vacuo*. Crystallisation of the residue from benzene (25 ml.) gave the fluorohydrin (XX) as needles (0·95 g., 30%), m. p. 228—231°, $[\alpha]_D$ +63° (Found: C, 65·5; H, 8·0; F, 4·3. Calc. for $C_{23}H_{33}O_6F$: C, 65·1; H, 7·8; F, 4·5%), $\nu_{max.}$ (in Nujol) 1732 and 1240 (OAc), and 1708 cm.$^{-1}$ (ketone), $\nu_{max.}$ (in $CHCl_3$) 3550—3400 (OH), 1740 (21-OAc), 1724 (20-ketone), and 1706 cm.$^{-1}$ (ketone). Hirschmann *et al.*[2a] give m. p. 233—233·5°, $[\alpha]_D$ +65·4° (in $CHCl_3$), and Fried *et al.*[2b] give m. p. 234—235°, $[\alpha]_D$ +67° (in acetone).

21-*Acetoxy*-2 : 4-*dibromo*-9α-*fluoro*-11β : 17-*dihydroxy*-5α-*pregnane*-3 : 20-*dione* (XXI).—Bromine (2·85 g.) in acetic acid (20 ml.) was added gradually during 10 min. to a stirred solution of the fluorohydrin (XX) (3·6 g.) in 0·675N-hydrogen bromide in acetic acid (81 ml.). After a further 20 min. at room temperature the solution was poured into water (700 ml.), the precipitated product was extracted into methylene chloride, and the extract was washed with aqueous sodium hydrogen carbonate and water. Removal of the solvent *in vacuo* from the dried extract left the crude 2 : 4-dibromo-compound as a pale yellow froth (5·1 g.).

21-*Acetoxy*-9α-*fluoro*-11β : 17-*dihydroxypregn*-4-*ene*-3 : 20-*dione* (XXII).—Bromine (0·46 ml.) was added to acetone (13 ml.) and, when the solution became colourless, sodium carbonate (1·2 g.) was added with stirring. When free from hydrogen bromide (30 min.) the solution was filtered, and the filtrate was added to a boiling suspension of sodium iodide (12·6 g.) in acetone (45 ml.). After 15 min. a solution of crude 21-acetoxy-2 : 4-dibromo-9α-fluoro-11β : 17-dihydroxy-5α-pregnane-3 : 20-dione (XXI) [2·55 g.; from 1·8 g. of (XX)] in acetone (11 ml.) was added and the mixture was boiled under reflux for 2 hr. The brown suspension was cooled and solid carbon dioxide added, before addition of an excess of 2N-chromous chloride (40 ml.). The suspension was allowed to warm to room temperature during 20 min., most of the acetone was removed *in vacuo*, and after dilution with water the product was extracted into methylene chloride. Removal of the solvent from the washed and dried extract left a pale yellow froth (1·7 g.), which was treated with acetic anhydride and pyridine at room temperature, in case some hydrolysis of the 21-acetoxy-group had occurred. The crude acetylated product, isolated with methylene chloride, had $\lambda_{max.}$ 239·5 mμ ($E^{1\%}_{1\,cm.}$ 153). It was boiled under reflux for 30 min. with Girard reagent P (0·9 g.) in dry ethanol (27 ml.) and acetic acid (1·35 ml.). The solution was cooled to 20°, 40% aqueous formaldehyde (3·6 ml.) was added, and, after 25 min., the solution was poured into aqueous 4% sodium hydrogen carbonate (135 ml.). The suspension was extracted with ethyl acetate, and the extract washed with aqueous sodium hydrogen carbonate and water. Removal of solvent from the dried extract left a yellow froth (890 mg.) (Found: F, 3·9%), which had $E^{1\%}_{1\,cm.}$ 37 at 235—240 mμ. The aqueous layers from the extraction were combined and acidified to pH 1 with 2N-hydrochloric acid. After 1 hr. the cloudy solution was extracted with ethyl acetate, and the extract was washed with aqueous sodium hydrogen carbonate and water. Removal of solvent from the dried extract left the crude product (XXII) as a yellow froth (685 mg.) (Found: F, 4·3%), $\lambda_{max.}$ 238·5 mμ ($E^{1\%}_{1\,cm.}$ 270).

This product (650 mg.) in benzene containing 5% chloroform (75 ml.) was chromatographed on acid-washed alumina (20 g.; Brockmann grade II—III). Benzene and up to 20% ether in

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benzene eluted mixtures (310 mg.) deficient in conjugated ketone. Elution with 1 : 4-ether–benzene and up to 1 : 1 chloroform–benzene gave crystalline fractions (180 mg. total), m. p. *ca.* 200—210° which, on crystallisation from ethyl acetate, gave the acetate (XXII) (114 mg., 6%) in two crops. Two interconvertible crystalline forms were obtained, both ethyl acetate solvates, of m. p. 205—208° and m. p. 222—227° respectively. The low-melting form had an infrared spectrum identical with that of an authentic sample with the higher melting point, $\nu_{max.}$ (in Nujol) 1750 and 1262 (21-acetate), 1718 (ketone), and 1642 and 878 cm.$^{-1}$ (conjugated ketone). Both of the forms were desolvated at 120°/0·1 mm., without change in m. p. (Found: C, 65·2; H, 7·1; F, 4·3. Calc. for $C_{23}H_{31}O_6F$: C, 65·4; H, 7·4; F, 4·5%). They had $[\alpha]_D$ +151° and $\lambda_{max.}$ 239 mμ (ε 15,900). The two desolvated forms had slightly different infrared spectra in bromoform, $\nu_{max.}$ 1740 and 1232 (21-OAc), 1722 (20-ketone), and 1658 and 1620 cm.$^{-1}$ (conjugated ketone and Δ^4), but differed considerably in Nujol. The differences in solution spectra could be accounted for by a trace of ethyl acetate in one of the samples. Fried and Sabo [18] give m. p. 232—233° (or 205—208° then 226—228°), $[\alpha]_D$ +143°, and $\lambda_{max.}$ 238 mμ (ε 16,800).

21-*Acetoxy*-9α-*fluoro*-11β : 17-*dihydroxypregna*-1 : 4-*diene*-3 : 20-*dione* (XXIII).—Crude 21-acetoxy-2 : 4-dibromo-9α-fluoro-11β : 17-dihydroxy-5α-pregnane-3 : 20-dione (XXI) [2·55 g.; from 1·8 g. of (XX)] and semicarbazide hydrochloride (2·5 g.) were heated under nitrogen at 100° for 90 min. in dimethylformamide (37 ml.) and water (2·5 ml.). After concentration *in vacuo* to *ca.* 15 ml., acetic acid (75 ml.), water (37 ml.), and 50% pyruvic acid (18 ml.) were added, and the mixture was heated under nitrogen at 100° for 90 min. The solution was poured into water (1 l.), and the product was isolated with methylene chloride as a yellow froth (880 mg.), $\lambda_{max.}$ 239 mμ ($E^{1\%}_{1\,cm.}$ 339). It was acetylated with acetic anhydride and pyridine at room temperature, and was then boiled under reflux with Girard reagent P (0·56 g.) in ethanol (16 ml.) and acetic acid (1·6 ml.). The cooled solution was poured into aqueous 4% sodium hydrogen carbonate (120 ml.), and the unchanged material was extracted into ethyl acetate. The solvent was removed *in vacuo* from the washed and dried extract, to give a yellow froth (637 mg.), $\lambda_{max.}$ 238 mμ ($E^{1\%}_{1\,cm.}$ 343) (Found: F, 3·4%). This crude material (620 mg.), in benzene containing 4% of chloroform (75 ml.), was chromatographed on acid-washed alumina (20 g.; Brockmann grade II—III). Elution with benzene gave a yellow gum (30 mg.) and then 20—30% ether-in-benzene eluted crude 21-acetoxy-9α-fluoro-11β-hydroxy-5α-pregna-1 : 4 : 16-triene-3 : 20-dione (180 mg.). Chloroform eluted a pale yellow gum (98 mg.) which, on crystallisation from ethyl acetate (1 ml.), gave, after drying at 100°/0·1 mm., the desired acetate (XXIII) (5 mg.), m. p. 220—228°, and a second crop (6 mg.), m. p. 223—231°, $\lambda_{max.}$ (in MeOH) 238 mμ (ε 15,400), $\nu_{max.}$ (in Nujol) 3450 and 3350 (OH), 1732 and 1270 (21-OAc), 1710 (ketone), 1660, 1618, 1600, and 890 cm.$^{-1}$ ($\Delta^{1:4}$-3-ketone). The literature [2] gives a range of constants, m. p. 235—238° to 244—246°, and $\lambda_{max.}$ *ca.* 239 mμ (ε 14,500—16,300).

3β-*Acetoxy*-9β : 11β-*epoxy*-17-*hydroxy*-5α-*pregnan*-20-*one* (XV; R = Ac).—3β : 17-Dihydroxy-5α-pregn-9(11)-en-20-one (5·0 g.), in dioxan (500 ml.) and water (75 ml.), was treated with *N*-bromoacetamide (5·0 g.) and aqueous 1·38% perchloric acid (77 ml.). After 20 min. at room temperature the excess of *N*-bromoacetamide was destroyed by addition of aqueous sodium pyrosulphite until the yellow colour disappeared. After addition of 2N-sodium hydroxide (125 ml.) and sufficient water (200 ml.) to give a single phase, the clear solution was left for 30 min. under nitrogen, and acidified with acetic acid. The dioxan was distilled *in vacuo* and, after addition of more water to the aqueous residue, the solid (2·94 g.) was filtered off. This material (2·8 g.) was acetylated with pyridine and acetic anhydride at 100°, and crystallised from aqueous methanol, to give the 9β : 11β-*epoxide* (1·88 g.) (34%), m. p. 163—169°, $[\alpha]_D$ +7·3°. Further crystallisation gave material with m. p. 174—176° and $[\alpha]_D$ +5·5° (Found: C, 70·8; H, 8·7. $C_{23}H_{34}O_5$ requires C, 70·7; H, 8·8%), $\nu_{max.}$ (in Nujol) 1722 and 1242 (OAc), 1695 (ketone), and 1354 cm.$^{-1}$ (CH_3·CO).

Hydrolysis of the acetate with potassium hydrogen carbonate in boiling aqueous methanol gave a crude product (94%) as plates, m. p. 254—260°. Crystallisation from methanol gave the 3β : 17-*diol* (XV; R = H) as prisms, m. p. 230—245°, with changes in crystalline form and decomposition, $[\alpha]_D$ +6° (*c* 0·35) (Found: C, 72·4; H, 9·2. $C_{21}H_{32}O_4$ requires C, 72·4; H, 9·3%). The infrared spectrum was the same as for the plates, $\nu_{max.}$ (in Nujol) 3360—3240 (OH) and 1702 and 1678 cm.$^{-1}$ (ketone).

9α-*Bromo*-11β-*hydroxyergostan*-3-*one* (XVII) (With Mr. G. F. H. Green).—Ergost-9(11)-en-3-one (5 g.) in dioxan (205 ml.) and water (23 ml.) was treated with *N*-bromoacetamide

(7·0 g.) and 60% perchloric acid (6·25 ml.). A yellow colour developed almost at once; after 2 min. just sufficient aqueous sodium pyrosulphite was added to remove the colour and the steroid solution was poured into water. The precipitated product (5·72 g., 93%), m. p. 112—114° (decomp.) (Found: Br, 15·0%), crystallised from *cyclo*hexane to give the *bromohydrin* (60%), m. p. 127—129° (decomp.) (capillary), $[\alpha]_D$ +38° (Found: C, 67·8; H, 9·6; Br, 15·5. $C_{28}H_{47}O_2Br$ requires C, 67·8; H, 9·6; Br, 16·1%), $\nu_{max.}$ (in CS_2) 3620 (OH), 1710 (ketone), and 748 cm.$^{-1}$ (C–Br).

The crude bromohydrin (500 mg.) was boiled for 1 hr. in ethanol, and the crude product (458 mg.) (Found: Br, 3·5%) was isolated by precipitation with water. Three crystallisations from aqueous acetone gave ergostane-3 : 11-dione (XIX) (131 mg.), m. p. 152—155°, $[\alpha]_D$ +63°, which appeared from its infrared spectrum (in CS_2) to contain a little of the 9β : 11β-epoxide. A similar result was obtained by boiling in the presence of two equivalents of potassium acetate.

9β : 11β-*Epoxyergostan-3-one* (XVIII) (With Mr. G. F. H. Green).—A solution of the foregoing bromohydrin (340 mg.) in dry *tert.*-butyl alcohol (20 ml.) was treated at room temperature during 0·5 min. with a solution of potassium *tert.*-butoxide [prepared from potassium (42·5 mg.) and *tert.*-butyl alcohol (4·6 ml.)]. After 5 min. the pale yellow cloudy solution was poured into water containing a little magnesium sulphate, and the precipitated product (290 mg.), m. p. 139—140°, $[\alpha]_D$ +30·5°, was crystallised twice from aqueous acetone, to give the *epoxide* (124 mg., 43%), m. p. 144—146°, $[\alpha]_D$ +32° (Found: C, 81·3; H, 11·2. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%), $\nu_{max.}$ (in CS_2) 1714 cm.$^{-1}$ (single ketone).

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808. *Technetium. Part I. The Preparation and Properties of Potassium Hexahalogenotechnetates.*

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Potassium hexa-chloro, -bromo-, and -iodo-technetates have been prepared. Their magnetic susceptibility, absorption spectra, and crystal structures are very similar to those of the corresponding rhenium compounds.

Technetium, the middle member of the Group VIIb triad, was first prepared [1] in 1937 but can now be isolated in relatively large amounts from the liquors produced when the slug from nuclear reactors is dissolved in nitric acid for purification. In the past few years elemental technetium has been characterised and its properties investigated; [2] also the oxides,[3] sulphides,[4] the tetrachloride,[4] and the heptavalent pertechnetates have been prepared and their magnetic properties examined. Nelson, Boyd, and Smith [3] have found that the quadrivalent dipotassium hexachlorotechnetate is isomorphous with the corresponding rhenium compound. They also studied the magnetic behaviour of the crystalline material over a range of temperature.

The position of technetium in the Periodic Table makes the magnetic and structural properties of its compounds of interest. Manganese forms spin-paired complexes with some reluctance whereas rhenium complexes are almost all of this type. From the work to date it appears that technetium bears a closer resemblance to rhenium than to manganese and hence it is to the former that one looks for a guide to its expected chemical behaviour.

All oxidation states of rhenium from −1 to +7 are now well established. The properties of many of these, *e.g.* rhenium(III) containing four non-bonding *d* electrons, are of interest in the light of ligand field theory. Unusual stereochemical arrangements are possible and the large spin–orbit coupling constants have interesting spectral and magnetic consequences. Since it falls between manganese, with a low spin–orbit coupling constant,

[1] Perrier and Segre, *J. Chem. Phys.*, 1937, **5**, 712; 1939, **7**, 155.
[2] Cobble, Nelson, Parker, Smith, and Boyd, *J. Amer. Chem. Soc.*, 1952, **74**, 1852.
[3] Nelson, Boyd, and Smith, *ibid.*, 1954, **76**, 348; see also *ibid.*, 1952, **74**, 556.
[4] Knox, Tyree, Srwastava, Norman, Bassett, and Holloway, *ibid.*, 1957, **79**, 3358.

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and rhenium with a large constant, technetium should show intermediate behaviour, possibly both magnetic susceptibility and stereochemistry being very sensitive to type of ligand. Since only 15 mg. of technetium as potassium technetate have been available to us, the following scheme of reactions, based on experience with rhenium, was designed to make the maximum use of the material:

$$KTcO_4 \xrightarrow[KI]{HCl} K_2TcCl_6 \xrightarrow[Evapn.]{HBr} K_2TcBr_6 \xrightarrow[Evapn.]{HI} K_2TcI_6$$

In this scheme the conversion of chlorotechnetate through the bromo-compound into iodotechnetate should be quantitative. Comparison of observed and calculated changes in molecular weight could therefore be used to follow the reactions to completion and so avoid the loss of samples to chemical analysis. The atomic weight of ^{99}Tc was estimated from packing-fraction data [5] to be about 98·9$_0$.

Potassium bromo- and iodo-technetates are indistinguishable from their rhenium analogues. Potassium chlorotechnetate shows the greatest divergence, being yellow (the chlororhenate is yellow-green). Purified potassium chlorotechnetate and bromotechnetate crystallise slowly from their strongly acid solutions in large regular octahedral crystals.

The *X*-ray powder photographs of potassium chlorotechnetate show that it is isomorphous with, but has a slightly smaller unit cell than, potassium chlororhenate. Table 1 summarises the results of these unit-cell measurements. This does not agree with the earlier work by Nelson, Boyd, and Smith but is in accordance with the expected trend, owing to the lanthanide contraction in this part of the Periodic Table. The lines missing from the powder photograph are such that potassium chlorotechnetate must have a face-centred cubic cell: probably with the same space-group ($0_h^5F_{M3M}$; $Z = 4$) as was derived by Aminoff [6] for potassium chlororhenate. Potassium bromotechnetate also has a face-centred cubic lattice with its unit cell slightly smaller than that of potassium bromorhenate. Potassium iodotechnetate has a non-cubic structure. Its powder pattern is almost identical with that of potassium iodorhenate. Morrow [7] has reported that the latter has orthorhombic symmetry with four formula weights in the unit cell. Fourteen of the seventeen lines in Guinier powder patterns of dry potassium iodorhenate can be indexed more satisfactorily with respect to a body-centred orthorhombic cell which contains two formula weights. The other three weak lines can be indexed when the related monoclinic cell, containing four formula weights, is used. The details of the body-centred orthorhombic pattern which have been found for potassium iodorhenate are given in Table 2.

TABLE 1. *Comparison of unit-cell dimensions of potassium halogeno-technetates and -rhenates (in* Å).

K_2TcCl_6	$a_0 = 9{\cdot}82(\pm 0{\cdot}01)$ [a] $a_0 = 9{\cdot}89$ [b]	K_2ReCl_6	$a_0 = 9{\cdot}82\ (\pm 0{\cdot}01)$ [a] $a_0 = 9{\cdot}842$ [b] $a_0 = 9{\cdot}861$ [c]
K_2TcBr_6	$a_0 = 10{\cdot}37(\pm 0{\cdot}02)$ [a]	K_2ReBr_6	$a_0 = 10{\cdot}38(\pm 0{\cdot}02)$ [a]
K_2TcI_6	$a = 11{\cdot}22$ $b = 8{\cdot}00$ $c = 7{\cdot}84$ } $\pm 0{\cdot}03$ Å	K_2ReI_6	$a = 11{\cdot}22$ $b = 8{\cdot}00$ $c = 7{\cdot}84$ } $\pm 0{\cdot}02$ Å $a = 11{\cdot}07(\pm 0{\cdot}05)$ [d] $b = 13{\cdot}48(\pm 0{\cdot}07)$ [d] $c = 10{\cdot}19(\pm 0{\cdot}05)$ [d]

[a] Present work. [b] Ref. 3. [c] Ref. 6. [d] Ref. 7.

The magnetic moments at room temperature of the halogenotechnetates in the corresponding halogen acid solutions are shown in Table 3. They decrease in the order $K_2TcI_6 > K_2TcCl_6 < K_2TcBr_6$, the discontinuity being just outside the experimental error. For solid hexachlorotechnetate Nelson, Boyd, and Smith report a moment of 4·3 B.M.

[5] Kaplan, "Nuclear Physics," Addison-Wesley Publ. Co. Inc., New York, 1955, 182.
[6] Aminoff, *Z. Kryst.*, 1936, *A*, **94**, 246.
[7] Morrow, *J. Phys. Chem.*, 1956, **60**, 19.

The hexahalogenotechnetates of technetium(IV) have an octahedral d_ϵ^3 configuration. This half-filled d_ϵ shell behaves essentially like an S spectroscopic state, equivalent to a half-filled p shell. The orbital angular momentum L in a cubic field of perfect octahedral symmetry should be effectively zero. As a result the moment should be given by the spin-only value of 3·88 B.M., obtained by putting S (total spin) $= 1\frac{1}{2}$ and $L = 0$ in the expression $\mu = [4S(S + 1) + L(L + 1)]^{\frac{1}{2}}$. The values shown in Table 2 are all slightly

TABLE 2. *Indices and approximate intensities of Guinier powder lines for potassium iodorhenate.* (Cu-K_α *radiation.*)

Intensity	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*hkl*	Intensity	$\sin^2\theta$ (obs.)	$\sin^2\theta$ (calc.)	*hkl*
s	0·0140	0·0141	110	m	0·0742	0·0758	022
		0·0145	101	s	0·0773	0·0773	400
m	0·0190	0·0190	011	w	0·0937	0·0932	031
m	0·0194	0·0193	200	m	0·0963	0·0963	411
w	0·0483	—	—			0·0964	013
mw	0·0516	0·0516	121	w	0·1221	—	—
m	0·0527	0·0528	112, 310	w	0·1261	0·1270	132, 330
		0·0532	301	m	0·1297	0·1291	123
s	0·0569	0·0565	220			0·1301	510
mw	0·0578	0·0581	202	w(b)	0·1509	0·1532	422
w	0·0667	—	—				

s = strong, m = medium, mw = medium weak, w = weak, (b) = broad line.

TABLE 3. *Magnetic moments* (μ_{eff}) *of potassium halogeno-technetates and -rhenates* (*in* B.M. *at* 20° *unless otherwise indicated*; *the Curie law is assumed to hold*).

	Chloride	Bromide	Iodide
Tc	4·05 ± 0·1	3·94 ± 0·1	4·14 ± 0·1
Re	3·30 (at 24°)	3·20 (at 22°)	3·57

[a] Klemm and Frischmuth, *Z. anorg. Chem.*, 1937, **230**, 220; Jensen, *ibid.*, 1944, **252**, 317. Measurements were made on solid rhenates; solutions of the halogenotechnetates were used: chloro- in 1 : 1-HCl; bromo- in 1 : 1-HBr, iodo- in constant-boiling HI.

in excess of this spin-only value for three unpaired electrons. However, with the limited amount of material available, we have had to carry out our measurements in aqueous solution and at one temperature only. Provided that there is no deviation from the perfect octahedral arrangement then according to Kotani's theory [8] the magnetic moment of 3·88 B.M. should be independent of temperature, with a Curie constant of zero. In fact, as is apparent with the corresponding rhenium(IV) complexes, some deviation from octahedral symmetry and/or exchange phenomena *via* halogen atoms can occur which affects the moment. With the larger amount of technetium shortly to be available we shall measure μ over a wide range of temperature.

TABLE 4. *Absorption bands* (*wavelengths in* Å) *and extinction coefficients* (*in parentheses*) *of rhenium and technetium compounds.*

K_2TcCl_6	7000(2·90)	K_2ReCl_6	7100(3·48), 6500(2·79)
K_2TcBr_6	11,300(1·10), 10,600(1·55), 7400(10·6)		
K_2ReBr_6	14,000(17·7), 11,200(23·9), 10,800(25·9), 7500(28·5), ~6700(double, 27·4)		

In Table 4 light-absorption details for chlorides and bromides of technetium and rhenium are compared. The spectrum of potassium chlorotechnetate in 1 : 1 hydrochloric acid is similar to that of potassium chlororhenate [9] but with a shift of the whole spectrum toward the longer wavelengths. Simple ligand field theory predicts that for an octahedral complex of this type two bands are to be expected in the visible or near-visible region, both corresponding with a transition of an electron from the d_ϵ to the d_γ level, *i.e.* the transition

[8] Kotani, *J. Phys. Soc. Japan*, 1949, **4**, 293.
[9] Jorgensen, *Acta Chem. Scand.*, 1955, **9**, 7102, and refs. therein.

$d_\epsilon^3 \longrightarrow d_\epsilon^2 d_\gamma^1$. (The two-electron transition leading to a $d_\epsilon^1 d_\gamma^2$ configuration would be at a much higher frequency.) With the complex bromides and iodides the two expected bands are observed at the frequencies and with the extinction coefficients shown in Table 3. However, only one band is observed with the $[TcCl_6]^{2-}$ ion between 4000—9000 Å. This is puzzling since the corresponding hexachlororhenate does show the expected two bands.

Experimental

Potassium Pertechnetate.—The starting material was 16 mg. of technetium as potassium pertechnetate solution. Potassium pertechnetate (32·2 mg.) was recovered from this by evaporation.

Potassium Chlorotechnetate.—Potassium pertechnetate (32·2 mg.) was dissolved in warm concentrated hydrochloric acid (5 ml.), and powdered potassium iodide (200 mg.) was added to reduce the technetium to the quadrivalent state. The liberated iodine was removed by concentrating the solution under an infrared lamp. After the solution had cooled, the remaining liquid, which contained little technetium, was decanted off. The brownish residue was dissolved in concentrated hydrochloric acid (20 ml.), and the solution allowed to simmer until its colour changed to pure yellow. After concentration of the solution yellow crystals appeared and the solution was allowed to cool. The first crop was practically pure but the second crop was contaminated with potassium chloride. Both crops were washed with acidified (HCl) methanol to remove potassium chloride and dried in a vacuum (yield 59·5 mg.). The yellow potassium chlorotechnetate was recrystallised from 2 ml. of concentrated hydrochloric acid (yield 43·6 mg., *i.e.* about 70%).

Molecular Weight of Potassium Bromotechnetate.—The recrystallised potassium chlorotechnetate (43·6 mg.) was converted into bromotechnetate by successive evaporation to dryness with portions (2 ml.) of concentrated hydrobromic acid (" AnalaR "). [Change in molecular weight: Found, 389·8 to 662·8. Calc., 389·8 to 656·6.]

Potassium Bromotechnetate.—The bromotechnetate, together with all the rejected chlorotechnetate solutions, was evaporated to dryness repeatedly with portions (3 ml.) of concentrated hydrobromic acid. The solution was finally concentrated to small bulk; reddish-brown crystals of potassium bromotechnetate then appeared. Next day the supernatant solution which contained only a little technetium was siphoned off and the potassium bromotechnetate recrystallised from the minimum of concentrated hydrobromic acid [yield 90·7 mg., *i.e.* about 87%].

Molecular Weight of Iodotechnetate.—Recrystallised potassium bromotechnetate (90·7 mg.) was evaporated to dryness with successive portions (1 ml.) of redistilled " AnalaR " hydriodic acid. After two evaporations the weight became constant. [Change in molecular weight: Found, 656·6 to 943·2. Calc., 656·6 to 938·6].

Potassium Iodotechnetate.—The iodotechnetate was combined with bromotechnetate recovered from residual solutions and evaporated to dryness with redistilled hydriodic acid (2 × 3 ml.). The product was dried and stored in a vacuum desiccator to avoid hydrolysis or oxidation [yield 124·7 mg., *i.e.* about 84%].

Rhenium Compounds.—An analogous set of molecular-weight determinations was carried out, ammonium chlororhenate being used as starting material. [Changes in molecular weight: Found, 435·3 to 702. Calc. for $(NH_4)_2ReCl_6$ to $(NH_4)_2ReBr_6$, 435·3 to 712·3. Found, 712·3 to 974. Calculated for $(NH_4)_2ReBr_6$ to $(NH_4)_2ReI_6$, 712·3 to 984·3.] Specimens of potassium halogenorhenates for *X*-ray measurements were prepared by standard methods.

X-Ray Photographs.—To avoid loss of material, and in the interests of safety, the vacuum-dried specimen was ground under dry benzene. The suspension was transferred by dropper to a wide-mouthed Pyrex capillary which was already filled with benzene. When the powdered specimen had settled the benzene was allowed to evaporate away. This method of preparing *X*-ray specimens also minimised possible hydrolysis or oxidation, especially of the iodotechnetate and iodorhenate. Photographs of the potassium halogenotechnetates were taken in 9-cm. cameras (Unicam Instruments Ltd.), cobalt radiation filtered through iron being used. A nickel screen was used next to the film in the camera to minimise the effects of β-radiation from the technetium.

Photographs of potassium iodorhenate were also taken in a Guinier-type camera (" Nonius," Delft), reflected cooper radiations being used. The method of sample mounting made this camera unsuitable for work with technetium.

Magnetic Susceptibilities.—These were determined by the Gouy method, approximately

4 ml. of 0·02—0·08M-solution being used. The column was 6·0 cm. long and the field strength 7000 gauss. The acid concentrations were: hydrochloric approx. 5N; hydrobromic approx. 5N; hydriodic approx. 8N. Owing to the high dilution, moments are considered correct to ±0·1 B.M.

Absorption Spectrum of Potassium Chlorotechnetate.—Measurements were made with a Perkin-Elmer self-recording Spectracord Type 4000. Solutions of chlororhenate and chlorotechnate were made up in 5—6N-hydrochloric acid. The corresponding bromo-compounds were made up in concentrated hydrobromic acid.

Health Precautions.—The manipulation of technetium on the milligram scale did not present a serious health hazard since ^{99}Tc is only a soft β emitter (0·3 Mev) with a specific activity, calculated from its half life of $2{\cdot}1 \times 10^5$ years,[10] of about 17 microcuries/mg.

Care was taken during the evaporation of strongly acid solutions of technetium, since there was possibility that some heptoxide might volatilise. Solutions were evaporated under infra-red lamps in a well-ventilated fume cupboard. The solution and its container were covered with a beaker which was removed and monitored from time to time.

The grinding of dry technetium compounds under benzene, to prevent their hydrolysis, has already been described. This method had the further advantage that it minimised the hazard from radioactive dust.

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[10] Fried, Yaffey, Hall, and Blendenin, *Phys. Rev.*, 1951, **81**, 741.

809. *Energy Levels of Planar Diphenyl.*

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A revision of London's [1] calculations on the lower π-electron energy levels of planar diphenyl gives results which provide a satisfactory quantitative correlation of the absorption spectra of diphenyl and benzene.

IN applying Goeppert-Mayer and Sklar's [2] method of antisymmetrized molecular orbitals to the quantitative interpretation of the absorption spectrum of diphenyl, London [1] formulated the spatial wave functions for the lower excited states not as twelve-factor products of one-electron molecular orbitals extending over the whole molecule, but as two-factor products of the six-electron total wave functions of the individual benzene rings.* He thus provided a means of estimating separately (*a*) the so-called π-electron energy levels of a hypothetical diphenyl molecule with a $C_{(1)}$–$C_{(1')}$ bond of infinite length (*i.e.*, the energy levels of two non-interacting benzene molecules, each in its own appropriate state of excitation); and (*b*) the changes in energy brought about by reducing the length of the $C_{(1)}$–$C_{(1')}$ bond from infinity to the equilibrium internuclear distance.

London rejected Goeppert-Mayer and Sklar's partially corrected values for (*a*) in favour of values related more closely to the absorption spectrum of benzene, and in so doing anticipated in some measure an argument which has become familiar recently as the basis of Moffitt's [3] modification of the method of antisymmetrized molecular orbitals. It is now recognized that, although Goeppert-Mayer and Sklar's technique in its original form (with the original atomic wave functions and the original Hamiltonian operator) may be expected

* Wave functions of the more conventional type have recently been used by Iguchi (*J. Phys. Soc. Japan*, 1937, **12**, 1250).

[1] A. London, *J. Chem. Phys.*, 1945, **13**, 396.
[2] Goeppert-Mayer and Sklar, *ibid.*, 1938, **6**, 645; Sklar and Lyddane, *ibid.*, 1939, **7**, 374.
[3] Moffitt, *Proc. Roy. Soc.*, 1951, *A*, **210**, 224, 245; 1953, *A*, **218**, 486; *Reports Progr. phys.*, 1954, **17**, 173; Moffitt and Scanlan, *Proc. Roy. Soc.*, 1953, *A*, **218**, 464; 1953, *A*, **220**, 530.

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to provide only a very poor approximation to the observed energy levels of an unsaturated hydrocarbon molecule, the same technique can often be employed fairly satisfactorily to calculate the relatively small energies of interaction between the constituent atoms or groups.

It is of interest in this connexion to investigate to what extent Goeppert-Mayer and Sklar's procedure succeeds in correlating the absorption spectrum of diphenyl with that of benzene; we therefore revised London's calculations, which incorporated a number of errors [4] and approximations carried over from earlier work.[2] The amended results are now presented.

For want of crystallographic data, the $C_{(1)}$–$C_{(1')}$ bond length in diphenyl is taken as 1·48 Å, and the other C–C bond lengths as 1·40 Å (cf. benzene [5]). If the central bond is extended indefinitely, the π-electron molecular orbitals of diphenyl degenerate into two identical sets of benzene orbitals, which, for either ring, can be written in the following real form: [6]

$$A = 0{\cdot}322053\ (\phi_1 + \phi_2 + \phi_3 + \phi_4 + \phi_5 + \phi_6)$$
$$B = 0{\cdot}456078\ (\phi_2 + \phi_3 - \phi_5 - \phi_6)$$
$$C = 0{\cdot}263317\ (2\phi_1 + \phi_2 - \phi_3 - 2\phi_4 - \phi_5 + \phi_6)$$
$$D = 0{\cdot}588307\ (\phi_2 - \phi_3 + \phi_5 - \phi_6)$$
$$E = 0{\cdot}339659\ (2\phi_1 - \phi_2 - \phi_3 + 2\phi_4 - \phi_5 - \phi_6)$$
$$F = 0{\cdot}553167\ (\phi_1 - \phi_2 + \phi_3 - \phi_4 + \phi_5 - \phi_6)$$
$$\left[\int \phi_1\phi_2 d\tau = 0{\cdot}256967;\ \int \phi_1\phi_3 d\tau = 0{\cdot}037898;\ \int \phi_1\phi_4 d\tau = 0{\cdot}017188\right]$$

The numeral subscripts conform with organic chemical usage: the atomic orbital ϕ_i is the $2p$-orbital of the carbon atom $C_{(i)}$ having its principal symmetry axis normal to the plane of the molecule. Where necessary in the following discussion, primes (′) will be used to distinguish the atomic or molecular wave functions of one ring from those of the other.

The lowest-energy molecular states [2] of each of the infinitely separated benzene rings are, in Craig's [7] notation:

$$\Phi_0 = 6^{-\frac{1}{2}}(|ABC\overline{ABC}|)$$
$$\Phi_1 = 24^{-\frac{1}{2}}(|\boldsymbol{ABC}\overline{\boldsymbol{ABD}}| + |\boldsymbol{ABC}\overline{\boldsymbol{ACE}}| \pm |\boldsymbol{ABD}\overline{\boldsymbol{ABC}}| \pm |\boldsymbol{ACE}\overline{\boldsymbol{ABC}}|)$$
$$\Phi_2 = 24^{-\frac{1}{2}}(|\boldsymbol{ABC}\overline{\boldsymbol{ABD}}| - |\boldsymbol{ABC}\overline{\boldsymbol{ACE}}| \pm |\boldsymbol{ABD}\overline{\boldsymbol{ABC}}| \mp |\boldsymbol{ACE}\overline{\boldsymbol{ABC}}|)$$
$$\Phi_3 = 24^{-\frac{1}{2}}(|\boldsymbol{ABC}\overline{\boldsymbol{ABE}}| + |\boldsymbol{ABC}\overline{\boldsymbol{ACD}}| \pm |\boldsymbol{ABE}\overline{\boldsymbol{ABC}}| \pm |\boldsymbol{ACD}\overline{\boldsymbol{ABC}}|)$$
$$\Phi_4 = 24^{-\frac{1}{2}}(|\boldsymbol{ABC}\overline{\boldsymbol{ABE}}| - |\boldsymbol{ABC}\overline{\boldsymbol{ACD}}| \pm |\boldsymbol{ABE}\overline{\boldsymbol{ABC}}| \mp |\boldsymbol{ACD}\overline{\boldsymbol{ABC}}|)$$

[Upper signs: singlet states. Lower signs: triplet states ($\sum m_s = 0$)]

Bars are used to differentiate between α and β spin factors; and for clarity the symbols for singly " occupied " orbitals are printed in bold-face type. The states Φ_1 and Φ_4 are degenerate.

The wave functions for the ground state and the lower excited π-electron states of a diphenyl molecule with an infinitely long central bond are, in non-normalized form:

$$\Psi_0 = \Phi_0\Phi_0';$$
$$\Psi_1 = \Phi_0\Phi_1' + \Phi_1\Phi_0';\ \Psi_5 = \Phi_0\Phi_3' + \Phi_3\Phi_0'$$
$$\Psi_2 = \Phi_0\Phi_1' - \Phi_1\Phi_0',\ \Psi_6 = \Phi_0\Phi_3' - \Phi_3\Phi_0'$$
$$\Psi_3 = \Phi_0\Phi_2' + \Phi_2\Phi_0';\ \Psi_7 = \Phi_0\Phi_4' + \Phi_4\Phi_0'$$
$$\Psi_4 = \Phi_0\Phi_2' - \Phi_2\Phi_0';\ \Psi_8 = \Phi_0\Phi_4' - \Phi_4\Phi_0'$$

[4] Parr and Crawford, *J. Chem. Phys.*, 1948, **16**, 1049.
[5] Cox, *Rev. Modern Physics*, 1958, **30**, 159.
[6] Coulson, " Valence," Oxford University Press, 1952, p. 240.
[7] Craig, *Proc. Roy. Soc.*, 1950, *A*, **200**, 474.

Appropriately antisymmetrized (Table 1), these functions can be used as zero-order functions in the calculation of the perturbation of the energy levels of planar diphenyl brought about by the reduction of the central-bond length from infinity to 1·48 Å. The resulting increments (ΔE) in the " vertical " excitation energies are listed in Table 2. It is of course impossible to assess the changes in the individual energy levels explicitly, for there is no obvious way of adapting Goeppert-Mayer and Sklar's approximation to provide a means of estimating the energy of repulsion between the carbon " cores " (nuclei plus σ-electrons).[8] Nor is it clear whether any allowance should be made for the difference between the potential of the $C_{(1)}$ and $C_{(1')}$ cores in diphenyl and the potential of the corresponding cores in benzene.

TABLE 1. *Wave functions for the lower excited states of diphenyl (non-normalized).*

Determinant	Coefficient of determinant in wave function Ψ_1	Ψ_2	Ψ_3	Ψ_4	Determinant	Coefficient of determinant in wave function Ψ_5	Ψ_6	Ψ_7	Ψ_8
$\lvert ABC\overline{A}\overline{B}\overline{C}A'B'\mathbf{C'}\overline{A'}\overline{B'}\overline{\mathbf{D'}}\rvert$	1	1	1	1	$\lvert ABC\overline{A}\overline{B}\overline{C}A'B'\mathbf{C'}\overline{A'}\overline{B'}\overline{\mathbf{E'}}\rvert$	1	1	1	1
$\lvert ABC\overline{A}\overline{B}\overline{C}A'\mathbf{B'}C'\overline{A'}\overline{C'}\overline{\mathbf{E'}}\rvert$	1	1	−1	−1	$\lvert ABC\overline{A}\overline{B}\overline{C}A'\mathbf{B'}C'\overline{A'}\overline{C'}\overline{\mathbf{D'}}\rvert$	1	1	−1	−1
$\lvert AB\mathbf{C}\overline{A}\overline{B}\overline{\mathbf{D}}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	1	−1	1	−1	$\lvert AB\mathbf{C}\overline{A}\overline{B}\overline{\mathbf{E}}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	1	−1	1	−1
$\lvert A\mathbf{B}C\overline{A}\overline{C}\overline{\mathbf{E}}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	1	−1	−1	1	$\lvert A\mathbf{B}C\overline{A}\overline{C}\overline{\mathbf{D}}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	1	−1	−1	1
$\lvert ABC\overline{A}\overline{B}\overline{C}A'B'\mathbf{D'}\overline{A'}\overline{B'}\overline{\mathbf{C'}}\rvert$	±1	±1	±1	±1	$\lvert ABC\overline{A}\overline{B}\overline{C}A'B'\mathbf{E'}\overline{A'}\overline{B'}\overline{\mathbf{C'}}\rvert$	±1	±1	±1	±1
$\lvert ABC\overline{A}\overline{B}\overline{C}A'C'\mathbf{E'}\overline{A'}\overline{\mathbf{B'}}\overline{C'}\rvert$	±1	±1	∓1	∓1	$\lvert ABC\overline{A}\overline{B}\overline{C}A'C'\mathbf{D'}\overline{A'}\overline{\mathbf{B'}}\overline{C'}\rvert$	±1	±1	∓1	∓1
$\lvert AB\mathbf{D}\overline{A}\overline{B}\overline{\mathbf{C}}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	±1	∓1	±1	∓1	$\lvert AB\mathbf{E}\overline{A}\overline{B}\overline{\mathbf{C}}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	±1	∓1	±1	∓1
$\lvert AC\mathbf{E}\overline{A}\overline{\mathbf{B}}\overline{C}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	±1	∓1	∓1	±1	$\lvert AC\mathbf{D}\overline{A}\overline{\mathbf{B}}\overline{C}A'B'C'\overline{A'}\overline{B'}\overline{C'}\rvert$	±1	∓1	∓1	±1

[Upper signs: singlet states. Lower signs: triplet states]

TABLE 2. *Transition energies of diphenyl in relation to those of benzene.*

Benzene: Excited state	Benzene: Symmetry (group D_{6h})	Benzene: Transition energy (obs.)	Diphenyl: Excited state	Diphenyl: Symmetry (group D_{2h})	Diphenyl: Polarization of allowed transition	Diphenyl: ΔE	Diphenyl: Transition energy (calc.)
		ev				ev	ev
$^1\Phi_1$	E_{1u}	**6·74** [a]	$^1\Psi_1$	B_{2u}	long.	0·3638	**7·10**
			$^1\Psi_2$	B_{1g}		−0·3320	6·41
$^1\Phi_2$	B_{2u}	4·88 [a]	$^1\Psi_3$	B_{2u}	long.	−0·0099	**4·87**
			$^1\Psi_4$	B_{1g}		0·0560	4·94
$^1\Phi_3$	B_{1u}	6·14 [a, b]	$^1\Psi_5$	A_g		0·1776	6·32
			$^1\Psi_6$	B_{3u}	trans.	−0·1750	**5·96**
$^1\Phi_4$	E_{1u}	**6·74**	$^1\Psi_7$	A_g		0·8244	7·56
			$^1\Psi_8$	B_{3u}	trans.	−0·8660	**5·87**
$^3\Phi_1$	E_{1u}	—	$^3\Psi_1$	B_{2u}		−0·0079	
			$^3\Psi_2$	B_{1g}		0·0531	
$^3\Phi_2$	B_{2u}	—	$^3\Psi_3$	B_{2u}		−0·0165	
			$^3\Psi_4$	B_{1g}		0·0497	
$^3\Phi_3$	B_{1u}	3·8 [c]	$^3\Psi_5$	A_g		0·0852	3·9
			$^3\Psi_6$	B_{3u}		−0·0410	3·8
$^3\Phi_4$	E_{1u}	—	$^3\Psi_7$	A_g		0·0872	
			$^3\Psi_8$	B_{3u}		−0·0119	

The symmetry notation is that of Longuet-Higgins and Murrell (ref. 12). The axes of polarization of the allowed transitions from the ground state are in the plane of the molecule: longitudinal = in the direction $C_{(1)}$–$C_{(1')}$; transverse = normal to the direction $C_{(1)}$–$C_{(1')}$. The energies of the allowed transitions are printed in bold-face type.

[a] Solution spectra.[9] [b] Symmetry uncertain (Dunn and Ingold, *Nature*, 1955, **176**, 65). [c] Symmetry uncertain (Shull, *J. Chem. Phys.*, 1949, **17**, 295; McClure, *ibid.*, p. 665; Craig, *ibid.*, 1950, **18**, 236).

Unlike that of benzene, the vapour-phase ultraviolet absorption spectrum of diphenyl has not been resolved into its component electronic transitions, and it is therefore difficult

[8] Cf. Craig, *Proc. Roy. Soc.*, 1950, *A*, **200**, 272 (see foot of p. 280).

[9] Klevens and Platt, Technical Report, Laboratory of Molecular Structure and Spectra, University of Chicago, 1953—54, I, 145.

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to decide how closely the allowed transitions at 4·87, 5·87, 5·96, and 7·10 ev suggested by the present calculations correspond with experimental data, especially as the overlapping of some of the transitions makes it impossible to attach very much quantitative significance to the directly observed intensity maxima. A comparison of the spectra of the two molecules measured under comparable conditions in fluorocarbon solutions,[9] however, shows that London's procedure offers a satisfactory interpretation of the grosser features of the spectrum of diphenyl, which are as follows. Covering much the same range as the forbidden 4·88 ev transition in benzene, there is a broad band of high intensity ($\varepsilon_{max.} \sim 18{,}000$). In the region of the 6·14 ev transition in benzene, but of higher intensity ($\varepsilon_{max.} \sim 52{,}000$) and rather wider range, there is a band with maxima at 6·0 ev and 6·2 ev, corresponding presumably to the calculated values of 5·87 ev and 5·96 ev. Finally there is a high-intensity transition of energy greater than 7·0 ev, outside the range of the solution spectrum,[10] confirming the quite substantial calculated displacement of the 6·74 ev benzene transition.

So little is known of the nature of the triplet states of diphenyl that it is not possible to comment on the second part of Table 2.

The calculations described here are of course restricted to planar diphenyl, and some disparity between theory and experiment is thus to be expected. In a study based on Pople's [11] extension of Hückel's empirical molecular-orbital method, Longuet-Higgins and Murrell [12,13] have examined the relation between the singlet levels of planar and perpendicular diphenyl and those of benzene, considering not only " locally excited " configurations (as in this paper), but also " charge-transfer " configurations produced by the excitation of an electron from a ground-state orbital of one benzene ring to a higher-energy orbital of the other.

For the locally excited configurations Longuet-Higgins and Murrell used wave functions of the type $\Phi_n \pm \Phi_{n'}$ ($n = 1, 2, 3, 4$). In view of this difference, and also the manifold differences in the methods of integral evaluation, it is pleasing to find a notable measure of agreement between the present results and those of the Cambridge authors. In Table 3 are listed the values of ΔE (ev) for the singlet states, (*a*) reproduced *seriatim* from Table 2, (*b*) derived from the final results of Longuet-Higgins and Murrell,[12] and (*c*) recalculated from Longuet-Higgins and Murrell's interaction matrices, the perturbation of the ground state and the locally excited configurations by the charge-transfer configurations being disregarded. [To facilitate comparison, the symbols which Longuet-Higgins and Murrell have adopted for the singlet excited states of benzene (α, p, β, β′) are given along with the orthodox symbols of group theory.]

TABLE 3.

Excited state of benzene	$^1E_{1u}$ (β)		$^1B_{2u}$ (α)		$^1B_{1u}$ (p)		$^1E_{1u}$ (β′)	
(*a*)	0·36	−0·33	−0·01	0·06	0·18	−0·18	0·82	−0·87
(*b*)	0·35	−0·37	0·08	0·09	0·32	−0·03	1·17	−1·40
(*c*)	0·38	−0·38	0·00	0·00	0·15	0·00	1·00	−1·15

Only in the last two columns is there a significant difference between (*a*) and (*b*); in each case half the difference is accounted for by charge-transfer effects. The overall agreement between the " empirical " and " non-empirical " results provides some justification for the use of Goeppert-Mayer and Sklar's computational technique in the calculation of relatively small interaction energies.

CALCULATIONS

Very few details need be given of the nature of the calculations, which essentially followed Parr and Crawford's [4,14] revision of Goeppert-Mayer and Sklar's procedure and departed from

[10] Carr and Stücklen, *J. Chem. Phys.*, 1936, **4**, 760.
[11] Pople, *Trans. Faraday Soc.*, 1953, **49**, 1375; *Proc. Phys. Soc.*, 1955, *A*, **68**, 81.
[12] Longuet-Higgins and Murrell, *ibid.*, p. 601.
[13] Murrell and Longuet-Higgins, *J.*, 1955, 2552.
[14] Parr and Crawford, *J. Chem. Phys.*, 1948, **16**, 526; Crawford and Parr, *ibid.*, 1949, **17**, 726.

established practice only in consequence of the lack of complete orthogonality between the two sets of one-electron benzene orbitals. Arising from this, all multiple exchanges were taken into account which could affect the calculated energies by more than 10^{-6} ev.

The carbon 2*s*-wave function was assumed to be of the same form [$r \exp(-1{\cdot}59r)$ in atomic units] as the radial factor of the 2*p*-wave functions. The well-known [3, 15] over-estimate of the one-centre Coulomb integral resulting from the use of unmodified atomic wave functions in molecular-orbital calculations, though of little consequence in a perturbation problem of the kind considered here, was avoided by the adoption of Pariser's [16] " empirical " value (10·53 ev) throughout, in the way suggested by Moser.[17] All relevant interactions between the twelve carbon " cores " and the twelve electrons were allowed for, three- and four-centre integrals of all types being evaluated by means of Mulliken's approximation.[18]

In determining the values of ΔE given in Table 2, no allowance was made for interaction between excited configurations of the same symmetry. The justification for applying the variation principle to π-electron wave functions is not immediately obvious,[19] especially when any empirical evaluation of integrals is involved; but if indeed the customary procedure [7] is adopted in the present calculations, the results suggest that the effect of configuration interaction is quite unimportant (ΔE changing by only 0·002—0·02 ev in the singlet states).

The computations were carried out in the Mathematical Institute of the University of Oxford in 1954—55 at Dr. L. E. Orgel's suggestion. The author thanks Professor C. A. Coulson, F.R.S., and Mr. V. W. Maslen for comments.

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[15] Pariser and Parr, *J. Chem. Phys.*, 1953, **21**, 466, 767.
[16] Pariser, *ibid.*, 1953, **21**, 568.
[17] Moser, *ibid.*, p. 2098.
[18] Mulliken, *J. Chim. phys.*, 1949, **46**, 500, 521; Rüdenberg, *J. Chem. Phys.*, 1951, **19**, 1433.
[19] C. A. Coulson, personal communication; cf. Lykos and Parr, *J. Chem. Phys.*, 1956, **24**, 1166; 1956, **25**, 1301.

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810. *Sisal Pectic Acid.*

By G. O. ASPINALL and A. CAÑAS-RODRIGUEZ.

Aqueous extraction of sisal flesh yields a mixture of polysaccharides, hydrolysis of which affords L-rhamnose, D-xylose, L-arabinose, D-glucose, D-galactose, and D-galacturonic acid, together with small amounts of 2-*O*-methyl-D-xylose and 2-*O*-methyl-L-fucose. Sisal pectic acid is subsequently extracted with ammonium oxalate. Reduction of the ethylene glycol ester of this pectic acid with potassium borohydride gives a galactan. Methylation studies indicate the presence in the pectic acid of chains of 1 : 4-linked α-D-galacturonic acid residues, but show that residues of L-rhamnose, L-arabinose, and D-galactose are also present.

PECTIC substances are usually mixtures of three polysaccharides: pectic acid, containing chains of 1 : 4-linked α-D-galacturonic acid residues, present mainly as methyl esters; a linear galactan containing chains of 1 : 4-linked β-D-galactopyranose residues; and a highly branched araban, containing 1 : 5- and 1 : 3-linked α-L-arabofuranose residues.[1] The proportions of the three polysaccharides vary in different pectins, but the components are very closely associated and it is not yet definitely known whether or not they are linked by covalent bonds. The structure of the acidic polysaccharide is based on methylation studies on pectic acid, which had been previously degraded with mineral acid to hydrolyse the associated neutral polysaccharides, and on the characterisation of the acidic di- and tri-saccharides formed on enzymic hydrolysis.[2] The present paper describes studies of

[1] Hirst and Jones, *Adv. Carbohydrate Chem.*, 1946, **2**, 235.
[2] Jones and Reid, *J.*, 1954, 1361; 1955, 1890.

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pectic acid isolated from the fleshy leaves of the sisal plant (*Agave sisalana*) in the mildest possible manner and without recourse to acidic reagents.

Extraction of sisal flesh with hot water gave a mixture of polysaccharides. Although fractional precipitation of this material from aqueous solution with acetone gave fractions differing in optical rotation, the same sugars were detected chromatographically on hydrolysis of the various fractions. One fraction was hydrolysed and the following sugars were identified after chromatographic separation on cellulose: L-rhamnose, D-xylose, L-arabinose, D-glucose, D-galactose, and D-galacturonic acid. In addition, very small amounts of two sugars with high chromatographic mobility were observed. In a separate experiment a larger quantity of the unfractionated water-soluble polysaccharide was hydrolysed, the products were adsorbed on charcoal, unsubstituted monosaccharides were eluted with water, and elution with ethanol–water mixtures followed by chromatography on filter sheets afforded 2-*O*-methyl-D-xylose and 2-*O*-methyl-L-fucose. These two sugars have recently been identified as constituents of plum leaf polysaccharides.[3]

Ammonium pectate was extracted from the sisal residue with hot ammonium oxalate solution, and hydrolysis of this material gave galacturonic acid, rhamnose, galactose, arabinose, and xylose. Regeneration of ammonium pectate after precipitation as the insoluble calcium salt resulted in removal of the xylose-containing moiety. Many subsequent attempts were made to fractionate the ammonium pectate, fractional precipitation from aqueous solution with acetone, precipitation *via* the calcium salt, and precipitation with cetyltrimethylammonium bromide,[4] but in no case was it possible to isolate a polygalacturonic acid devoid of neutral sugars. Indeed, the regenerated ammonium pectates were almost unchanged in optical rotation and uronic anhydride content, and gave on hydrolysis galacturonic acid, together with rhamnose, galactose, and arabinose.

Ammonium pectate was treated with methyl sulphate and sodium hydroxide, the methylated sodium pectate was converted into the silver salt, and treatment with methyl iodide afforded the methyl ester. In order to remove associated neutral methylated polysaccharide the methylated methyl pectate was saponified with cold ethanolic sodium hydroxide, and the precipitated methylated sodium pectate was separated and reconverted into methylated methyl pectate. Hydrolysis of the methylated polysaccharide, together with reduction of uronic acid to hexose residues was carried out in the following manner. Methylated methyl pectate was heated in a sealed tube at 100° with methanolic hydrogen chloride, the methanolysis product was reduced with lithium aluminium hydride in tetrahydrofuran solution, and the reduction product was hydrolysed in aqueous solution. The resulting mixture of sugars was separated on cellulose, to give 2 : 3-di-*O*-methyl-D-galactose as the main component, together with smaller amounts of 2 : 3 : 4-tri- and 3 : 4-di-*O*-methyl-L-rhamnose, and 2 : 3 : 4 : 6-tetra-, 2 : 3 : 4- and 2 : 3 : 6-tri-, 2 : 4-di -,and 2-mono-*O*-methyl-D-galactose. In addition, there was chromatographic evidence for 2 : 3 : 5-tri-*O*-methylarabinose and 3-*O*-methylgalactose.

It is clear from these results that the main component, 2 : 3-di-*O*-methyl-D-galactose, has arisen from residues of 2 : 3-di-*O*-methyl-D-galacturonic acid, and that sisal pectic acid contains chains of 1 : 4-linked α-D-galacturonic acid residues. It is possible that the 2 : 3 : 4-tri-*O*-methyl-D-galactose originates from a non-reducing D-galacturonic acid end group. The 2 : 3 : 4-tri- and 3 : 4-di-*O*-methyl-L-rhamnose, and 2 : 3 : 4 : 6-tetra- and 2 : 3 : 6-tri-*O*-methyl-D-galactose, however, must arise from L-rhamnose and D-galactose residues originally present as polysaccharide components. Although it was not possible to estimate accurately the amounts of these methylated sugars, the high proportion of both these sugars present as non-reducing end groups can only be explained if these sugars are attached in some way to D-galacturonic acid residues.

In another series of experiments sisal pectic acid was converted into the ethylene glycol

[3] Andrews and Hough, *Chem. and Ind.*, 1956, 1278; Anderson, Andrews, and Hough, *ibid.*, 1957, 1453.

[4] Bera, Foster, and Stacey, *J.*, 1955, 3788.

ester by reaction with ethylene oxide.[5] A similarly prepared propylene glycol ester [5] had a molecular weight (from sedimentation and diffusion measurements) of 37,200, corresponding to a degree of polymerisation of 169. The ethylene glycol ester was reduced with potassium borohydride in aqueous solution in the presence of glycerol, which maintained the pH of the solution at about 8 and minimised alkaline hydrolysis of the ester.[6] Although it was not possible to obtain a completely reduced polysaccharide by this means, after repeated esterification and reduction a polysaccharide containing only 5—6% of uronic anhydride was isolated. Hydrolysis of this material gave galactose (77%), arabinose (6·5%), rhamnose (3%), and glucose (2%). A molecular-weight determination (from sedimentation and diffusion measurements) gave a value of 22,100, corresponding to a degree of polymerisation of 139. A comparison of this value with that obtained for the pectic acid propylene glycol ester shows that potassium borohydride reduction causes very little degradation.

A less completely reduced pectic acid (uronic anhydride, 18%) was methylated and complete reduction of uronic acid groups was effected by treatment of the methylated polysaccharide with lithium aluminium hydride in tetrahydrofuran. Further methylation of the reduction product afforded methylated galactan. Hydrolysis of the methylated polysaccharide gave 2 : 3 : 5-tri-*O*-methyl-L-arabinose, 2 : 3 : 4 : 6-tetra- and 2 : 3 : 6-tri-*O*-methyl-D-galactose, and a mixture of di-*O*-methyl-D-galactoses, the 2 : 4-isomer being definitely characterised. The isolation of 2 : 3 : 6-tri-*O*-methyl-D-galactose as the main product of hydrolysis is consistent with the presence of chains of 1 : 4-linked α-D-galacturonic acid residues in the original pectic acid. Since L-arabinose was found only as non-reducing end groups in the furanose form, this sugar cannot occur as an araban of the type found in other pectic materials [1] and must be present as a constituent of a polysaccharide in which D-galacturonic acid or D-galactose residues form the framework of the molecular structure.

It is not possible to draw precise conclusions regarding the structure of sisal pectic acid from these experiments. The pectic acid is composed of chains of 1 : 4-linked α-D-galacturonic acid residues, but the rôle of the neutral sugars, D-galactose, L-rhamnose, and L-arabinose, in the polysaccharide structure is not yet clear. In view of the tenacity of the association of these neutral sugars with the D-galacturonic acid residues, it seems probable that they are constituents of acidic rather than neutral polysaccharides. Two possibilities may be suggested on the basis of present evidence: (*a*) that these sugars are constituents of pectic acid and are linked to the galacturonic acid chains; or (*b*) that there is present a mixture of acidic polysaccharides, one composed solely of D-galacturonic acid residues and the other or others containing both neutral sugar and D-galacturonic acid residues. It is possible that pectic substances, like the hemicelluloses, contain a series of closely related molecular species.

Experimental

Paper partition chromatography was carried out on Whatman No. 1 filter paper with the following solvent systems (v/v): (A) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3, upper layer); (B) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (C) butan-2-one, half saturated with water containing 1% of ammonia; (D) ethyl acetate–acetic acid–water (3 : 1 : 3, upper layer); (E) butan-1-ol–acetic acid–water (4 : 1 : 5, upper layer); (F) ethyl acetate–pyridine–water (10 : 4 : 3); (G) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4); (H) benzene–ethanol–water (169 : 47 : 15, upper layer); (J) butan-2-one–acetic acid–water (9 : 1 : 1), saturated with boric acid. Unless otherwise stated, R_G values of methylated sugars refer to rates of movement relative to tetra-*O*-methyl-D-glucose in solvent B. Chromatography of the periodate oxidation products of methylated sugars was carried by Lemieux and Bauer's

[5] Deuel, *Helv. Chim. Acta*, 1947, **30**, 1523.
[6] Deuel and Zweifel, unpublished results (we are most grateful to Dr. G. Zweifel for furnishing us with experimental details in advance of publication).

method.[7] Methylated sugars were demethylated with hydrobromic acid.[8] Optical rotations were observed at 18° ± 2°.

Isolation and Examination of the Water-soluble Polysaccharides.—Sisal flesh (the fleshy part of the plant from which the fibre has been removed; 1 kg.) was extracted with water (6 l.) at 90° for 3 hr. After filtration and centrifugation the extract was concentrated to 1 l. and poured into an equal volume of acetone to give a crude polysaccharide mixture (*ca.* 20 g.). This material was dissolved in water (400 ml.), and acetone (400 ml.) was added slowly with stirring to the solution to give fraction *a* {14·7 g., $[\alpha]_D$ +74° (*c* 0·11 in H_2O), uronic anhydride (Kaye and Kent's method,[9] 32%}. Addition of further quantities of acetone to the supernatant liquid gave fractions *b* (2·5 g.), $[\alpha]_D$ −19° (*c* 0·21 in H_2O), and *c* (1·3 g.), $[\alpha]_D$ +47° (*c* 0·17 in H_2O). Hydrolysis of samples of the polysaccharide fractions gave galactose, glucose, arabinose, xylose, rhamnose, and traces of two minor components.

Water-soluble polysaccharide (fraction *a*, 1·84 g.) was heated with N-sulphuric acid 100 ml.) at 100° for 4 hr., the cooled solution was neutralised with barium carbonate, and the filtrate was concentrated to a syrup (1·70 g.). The syrup (1·57 g.) was fractionated on a cellulose column with butan-1 ol, half saturated with water, as eluant to give six fractions, and a seventh fraction was obtained by elution with water. Fraction 1 (27 mg.) contained a sugar (R_G 0·42 in solvent B) chromatographically and ionophoretically indistinguishable from 2-*O*-methyl-D-xylose and two minor components with R_G 0·57 and 0·73. Fraction 2 (105 mg.), $[\alpha]_D$ +8·6° (*c* 1·0 in H_2O), was identified as L-rhamnose by conversion into the benzoylhydrazone, m. p. and mixed m. p. 180—181°. Fraction 3 (47 mg.), $[\alpha]_D$ +19·2° (*c* 0·4 in H_2O), was identified as D-xylose by conversion into the di-*O*-benzylidene dimethyl acetal, m. p. and mixed m. p. 210—211°. Fraction 4 (202 mg.), $[\alpha]_D$ +106° (*c* 2·0 in H_2O), was identified as L-arabinose by conversion into the benzoylhydrazone, m. p. and mixed m. p. 185—189°. Chromatography of fraction 5 (300 mg.) showed glucose and galactose, and the presence of D-glucose was confirmed by the formation of the *p*-nitrophenylhydrazone, m. p. 184—185° and mixed m. p. 183—185°. The optical rotation of fraction 5, $[\alpha]_D$ +57·4° (*c* 1·6 in H_2O), corresponded to the presence of D-glucose (236 mg.) and D-galactose (64 mg.). Fraction 6 (130 mg.), $[\alpha]_D$ +81° (*c* 1·3 in H_2O), was identified as D-galactose by conversion into the 1-methyl-1-phenylhydrazone, m. p. and mixed m. p. 187—189°. Fraction 7 (665 mg.), obtained as barium salt, was treated with Amberlite resin IR-120(H) to give D-galacturonic acid, $[\alpha]_D$ +84·5° (*c* 1·7 in H_2O), identified as the 2 : 5-dichlorophenylhydrazone, m. p. and mixed m. p. 179—181°, and by conversion into mucic acid, m. p. and mixed m. p. 205—206°.

Isolation of 2-O-*Methyl*-D-*xylose and* 2-O-*Methyl*-L-*fucose.*—The unfractionated polysaccharide mixture (10 g.) was hydrolysed with N-sulphuric acid (500 ml.) at 100° for 6 hr., and the cooled solution was neutralised with barium carbonate, filtered, treated with Amberlite resin IR-120(H) to remove barium ions, concentrated, and absorbed on charcoal. The column was eluted successively with water and water containing increasing proportions of ethanol. A fraction (*ca.* 100 mg.), eluted with water containing 15% of ethanol, contained rhamnose, and sugars *a* and *b* with R_G 0·42 and 0·57. Pure samples of these sugars were isolated after chromatography on filter sheets with solvent 5. Sugar *a* (45 mg.) was identified as 2-*O*-methyl-D-xylose by m. p. 132—134° and mixed m. p. 131—133°, $[\alpha]_D$ +34° ± 1° (equil.) (*c* 0·25 in H_2O), and *X*-ray powder photograph. Sugar *b* (18 mg.) was identified as 2-*O*-methyl-L-fucose by m. p. 154—159° and mixed m. p. 155—159°, $[\alpha]_D$ −85° ± 1° (equil.) (*c* 0·36 in H_2O), and *X*-ray powder photograph. Chromatography of the periodate-oxidation products of both sugars showed methoxymalondialdehyde.

Isolation of Sisal Pectic Acid.—Water-extracted sisal flesh (2 kg.) was extracted five times with 0·5% ammonium oxalate solution (10 l.) at 80—90° for 2 hr. The extracts were concentrated to 2 l. and crude ammonium pectate was precipitated by the addition of an equal volume of ethanol. Calcium chloride solution (5%) was added to a 2% aqueous solution of this material until no further precipitate was formed, and the calcium pectate was then separated. A sample of calcium pectate was hydrolysed; chromatography then showed rhamnose, xylose, arabinose, galactose, and galacturonic acid. Calcium pectate was suspended in water and heated at 80° for 1 hr. with a slight excess of ammonium oxalate, calcium oxalate was removed by filtration, and the solution was dialysed against distilled water. Hydrolysis of an aliquot

[7] Lemieux and Bauer, *Canad. J. Chem.*, 1953, **31**, 814.
[8] Hough, Jones, and Wadman, *J.*, 1950, 1705.
[9] Kaye and Kent, *J.*, 1953, 79.

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part gave the same mixture of sugars but no xylose. After a second precipitation of the polysaccharide as calcium salt, it was isolated as ammonium salt by freeze-drying (yield, 180 g.). A sample of ammonium pectate in aqueous solution was passed through a column of Amberlite resin IR-120(H) and the derived pectic acid had $[\alpha]_D$ +238° (*c* 0·57 in H_2O) [Found: uronic anhydride (by decarboxylation), 77·1%; equiv., 233 (corresponds to 75·6% of uronic anhydride)].

Attempted Fractionations of Ammonium Pectate.—(1) Sodium hydroxide (10 g.) in water (20 ml.) was added to a suspension of crude ammonium pectate (20 g.) in ethanol (450 ml.), and the mixture was kept at 0° for 40 hr. with occasional shaking. The solid was filtered off, washed thoroughly with ethanol–water (1 : 1) to remove alkali, and reprecipitated twice from aqueous solution by the addition of an equal volume of ethanol. The resulting sodium pectate was extracted twice for 1 hr. with boiling ethanol–water (1 : 1), dissolved in water, precipitated as calcium pectate, and isolated as above by conversion into ammonium pectate (sample A), $[\alpha]_D$ +213° (*c* 0·83 in H_2O) [Found: uronic anhydride (by decarboxylation), 75·2%]. Hydrolysis of a sample gave rhamnose, arabinose, galactose, and galacturonic acid.

(2) A 10% aqueous solution of "Cetavlon" (cetyltrimethylammonium bromide) was added to ammonium pectate (25 g.) in water (1·2 l.), and the precipitated polysaccharide complex was separated at the centrifuge. The complex was decomposed by stirring it with 5N-acetic acid and pouring the mixture into 3 vol. of ethanol. Since the precipitated polysaccharide contained adhering "Cetavlon," it was redispersed in water, shaken for 2 hr. with Amberlite resin IR-120(H), filtered, and freeze-dried, to give pectic acid (sample B; 20 g.), $[\alpha]_D$ +215° (as ammonium salt) (*c* 0·4 in H_2O) [Found: uronic anhydride (by decarboxylation), 79·0%]. Hydrolysis of a sample gave rhamnose, arabinose, galactose, and galacturonic acid.

(3) Crude ammonium pectate (20 g.) was dissolved in water (1 l.) and precipitated by the addition of an equal volume of acetone. After a second reprecipitation the polysaccharide was extracted twice with boiling ethanol–water (1 : 1), dissolved in water, and isolated by freeze-drying. Ammonium pectate (15 g.) had $[\alpha]_D$ +213° (*c* 1·0 in H_2O) [Found: uronic anhydride, 74·0%]. Hydrolysis of a sample gave rhamnose, arabinose, galactose, and galacturonic acid.

Methylation of Ammonium Pectate.—Ammonium pectate (sample A, 20 g.) was methylated with methyl sulphate and sodium hydroxide, and the product was isolated as methylated sodium pectate (OMe, 22·6%). The sodium salt after extraction with methanol to remove neutral polysaccharides was dissolved in water, the solution was passed through a column of Amberlite resin IR-120(H) to remove sodium ions, and the resulting acid was converted into silver salt by treatment with silver oxide. Finely ground silver salt was refluxed with methyl iodide containing 5% of methanol, silver oxide (50 g.) was added during 4 hr., and refluxing was continued for a further 4 hr. After a further treatment with methyl iodide and silver oxide the methylated polysaccharide (10·5—11 g.) was isolated, $[\alpha]_D$ +191° (*c* 0·63 in $CHCl_3$) (Found: OMe, 39·4%).

Purification of Methylated Methyl Pectate.—Light petroleum (b. p. 40—60°) (285 ml.) was added to a solution of the methylated polysaccharide (8·1 g.) in chloroform (135 ml.), and the precipitated material (6·7 g.) was separated. This fraction was dissolved in ethanol (100 ml.), sodium hydroxide (4 g.) in water (4 ml.) was added dropwise with stirring, and the mixture was left at 0° for 8 hr. Ethanol–ether (1 : 1; 100 ml.) was added to the mixture, and the gelatinous precipitate was separated at the centrifuge and washed with ethanol–ether (1 : 1) until free from alkali. The methylated sodium pectate was then converted into the silver salt as described previously, and after treatment with methyl iodide and silver oxide afforded methylated methyl pectate (5 g.), $[\alpha]_D$ +212° (*c* 0·4 in $CHCl_3$) (Found: OMe, 40·0%).

Methanolysis of Methylated Methyl Pectate; Reduction, Hydrolysis, and Separation of Methylated Sugars.—Methylated methyl pectate (5 g.) was heated in a sealed tube with methanolic 4% hydrogen chloride (100 ml.) at 100° for 4 hr. After neutralisation with silver carbonate and removal of solvent, the resulting syrup was dissolved in tetrahydrofuran (150 ml.), and lithium aluminium hydride (2 g.) in tetrahydrofuran (50 ml.) was added dropwise during 1 hr. to the boiling solution. The mixture was refluxed for 1 hr., then set aside at room temperature for 2 hr., excess of hydride was destroyed by addition of water, and the mixture was taken to dryness. The residue was exhaustively extracted with acetone and ethanol, the extracts were diluted with water, de-ionised with Amberlite resins IR-120(H) and IR-4B(OH), evaporated, and hydrolysed with N-hydrochloric acid at 100° for 5 hr., to give a syrupy mixture of sugars (3·66 g.).

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The mixture of sugars was separated on cellulose by using solvent B. Only one pure sugar was obtained and the remaining fractions, which all contained several components, were recombined. The pure sugar (2·0 g.) had $[\alpha]_D$ +80° (*c* 0·63 in H_2O) (Found: OMe, 29·9. Calc. for $C_8H_{16}O_6$: OMe, 29·8%) and was characterised as 2 : 3-di-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 154—155°, and into 2 : 3-di-*O*-methyl-D-galactonamide, m. p. and mixed m. p. 139—140°. The remaining fractions (1·23 g.) were refractionated on cellulose (70 × 2·5 cm.) with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3) saturated with water as eluant to give thirteen fractions.

Fraction 1. The chromatographically pure syrup (23 mg.) had $[\alpha]_D$ +25° (*c* 0·2 in H_2O) and R_G 1·01. Demethylation gave rhamnose. In a separate experiment the sugar was characterised as 2 : 3 : 4-tri-*O*-methyl-L-rhamnose by conversion into 2 : 3 : 4-tri-*O*-methyl-L-rhamnonophenylhydrazide, m. p. 175—177°.

Fraction 2. Chromatography of the syrup (134 mg.) showed two components, R_G 0·95 and 0·90, and the optical rotation, $[\alpha]_D$ +49° (*c* 1·6 in H_2O), was consistent with the presence of 2 : 3 : 5-tri-*O*-methyl-L-arabinose (50 mg.) and 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose (84 mg.) in the mixture. Demethylation gave arabinose and galactose.

Fraction 3. The chromatographically pure syrup (19 mg.) had $[\alpha]_D$ +108° (*c* 0·18 in H_2O) and R_G 0·90 and was characterised as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 187—190°.

Fraction 4. Chromatography of the syrup (86 mg.) showed two components, R_G 0·90 and 0·88, together with traces of slower-moving substances. Quantitative chromatography [10] (separation in solvent H) indicated the presence of tetra-*O*-methylgalactose (27 mg.) and di-*O*-methylrhamnose in the mixture. Demethylation gave galactose and rhamnose. 2 : 3 : 4 : 6-Tetra-*O*-methyl-D-galactose was characterised as the aniline derivative, m. p. and mixed m. p. 189—191°. Ionophoresis showed the rhamnose derivative to be the 3 : 4-dimethyl ether. In a separate experiment this sugar was characterised by conversion into 3 : 4-di-*O*-methyl-L-rhamnonolactone, m. p. 76—78°.

Fraction 5. Chromatography of the sugar (137 mg.) showed a main component, R_G 0·78, and a trace of 2 : 3 : 6-tri-*O*-methylgalactose. Demethylation gave galactose. Since further hydrolysis gave 2 : 3-di-*O*-methylgalactose as the major product, it is probable that the main component is a polymer of 2 : 3-di-*O*-methylgalactose resulting from incomplete hydrolysis of the methylated polysaccharide.

Fraction 6. The sugar (18 mg.), $[\alpha]_D$ +111° (*c* 0·35 in H_2O, R_G 0·70) was identified as 2 : 3 : 4-tri-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 163—165°.

Fraction 7. Chromatography of the syrup (47 mg.), $[\alpha]_D$ +85° (*c* 0·61 in H_2O), showed 2 : 3 : 6-tri-*O*-methylgalactose (R_G 0·72) and a small amount of the 2 : 3 : 4-isomer (R_G 0·69). The main component was characterised by conversion into 2 : 3 : 6-tri-*O*-methyl-D-galactonolactone, m. p. and mixed m. p. 98—99°.

Fraction 8. Chromatography of the syrup (54 mg.), $[\alpha]_D$ +86° ± 2° (*c* 0·9 in H_2O), showed two components, R_G 0·76 and 0·64. Quantitative chromatography [10] indicated the presence of 2 : 3 : 6- (24 mg.) and (probably) 2 : 3 : 4-tri-*O*-methylgalactose (29 mg.) in the mixture. Demethylation gave galactose.

Fraction 9. Quantitative chromatography [10] of the syrup (65 mg.) showed two main components, R_G 0·64 (probably 2 : 3 : 4-tri-*O*-methylgalactose) (45 mg.) and 0·50 (di-*O*-methylgalactose) (19 mg.), and a trace of 2 : 3 : 6-tri-*O*-methylgalactose. Chromatography of the periodate oxidation products of the di-*O*-methylgalactose fraction indicated the presence of the 2 : 3- and the 2 : 6-dimethyl ether.

Fraction 10. The syrup (38 mg.) had $[\alpha]_D$ +83° (*c* 0·67 in H_2O) and R_G 0·56. Chromatography in solvent C showed a mixture of 2 : 4- (R_G 0·2) and 2 : 3(and possibly 2 : 6)-di-*O*-methylgalactose (R_G 0·3). Chromatography of the periodate-oxidation products indicated the presence of 2 : 3-, 2 : 4-, and 2 : 6-di-*O*-methylgalactose. The presence of 2 : 4-di-*O*-methyl-D-galactose in the mixture was confirmed by the formation of the aniline derivative, m. p. 208—209·5°.

Fraction 11. The syrup (31 mg.), $[\alpha]_D$ +81°, contained a main component (R_G 0·50) and traces of two minor components (R_G 0·72 and 0·42). The main component was identified as

[10] Hirst, Hough, and Jones, *J.*, 1949, 928.

2 : 3-di-*O*-methyl-D-galactose by conversion into the aniline derivative, m. p. and mixed m. p. 152—154°.

Fraction 12. The syrup (38 mg.) contained a complex mixture of sugars (R_G 0·88, 0·70, 0·43, and 0·38) and was not examined further.

Fraction 13. Quantitative chromatography in solvent C indicated the presence of 2-*O*-methylgalactose (192 mg.), 3-*O*-methylgalactose (113 mg.), and galactose (14 mg.). Chromatography of the periodate oxidation products showed methoxymalondialdehyde (from 2-*O*-methylaldoses) and a methylated pentose (probably 2-*O*-methyl-lyxose from 3-*O*-methylgalactose). After separation of part of the fraction on filter sheets with solvent J, 2-*O*-methyl-D-galactose, m. p. and mixed m. p. 150—154°, was isolated.

Preparation of Ethylene Glycol Pectate.—Ethylene oxide (100 ml.) was added to a suspension of pectic acid (sample, B; 33 g.) in water (330 ml.), and the mixture was shaken at room temperature for 9 days, until the resulting solution was neutral. The glycol ester was precipitated by the addition of acetone, redispersed in water, and isolated by freeze-drying. The glycol ester (39 g.) had $[\alpha]_D$ +193° ± 3° (*c* 0·59 in H_2O) [Found: uronic anhydride (by decarboxylation), 65% (≡ 78% uronic anhydride in pectic acid); equiv., 263 (≡ 67% uronic anhydride in glycol ester and 80% uronic anhydride in pectic acid); glycol released on saponification, 67·5% (≡ 81% uronic anhydride in pectic acid)].

Preparation of Propylene Glycol Pectate.—Similarly reaction of propylene oxide with pectic acid afforded propylene glycol pectate, $[\alpha]_D$ +168° ± 2° (*c* 0·89 in H_2O) [Found: uronic anhydride (by decarboxylation), 62% (≡ 78% in pectic acid); glycol released on saponification, 63·5% (≡ 80% uronic anhydride in pectic acid)]. Sedimentation and diffusion measurements gave a weight-average molecular weight of 37,200, corresponding to a degree of polymerisation of 169 ($S = 1{\cdot}5 \times 10^{-13}$; $D = 2{\cdot}5 \times 10^{-7}$; $\bar{v} = 0{\cdot}6$).

Reduction of Ethylene Glycol Pectate.—Potassium borohydride (3·5 g.) in water (20 ml.) was added to ethylene glycol pectate (11 g.) in water (250 ml.) containing glycerol (4·5 g.) at 0°. After being kept overnight the solution was de-ionised by passage through columns of Amberlite resins IR-120(H) and IRA-400(OH) and the partially reduced polysaccharide (7·3 g.) was isolated by freeze-drying. The derived ethylene glycol ester had $[\alpha]_D$ +247° (*c* 0·33 in H_2O) [Found: uronic anhydride (Kaye and Kent's method [9]), 18·4% (≡ 19·3% uronic anhydride in polysaccharide acid)]. After five further reductions the resulting galactan (5 g.) had $[\alpha]_D$ +247° (*c* 1·3 in H_2O) [Found: uronic anhydride, 5·0% (by decarboxylation); 5·9% (Kaye and Kent's method [9])]. A sample was hydrolysed and quantitative chromatography [11] showed galactose (77%), arabinose (6·5%), rhamnose (3%), and glucose (2%). Sedimentation and diffusion measurements gave a weight-average molecular weight of 22,100, corresponding to a degree of polymerisation of 139 ($S = 1{\cdot}42 \times 10^{-13}$; $D = 4{\cdot}0 \times 10^{-7}$; $\bar{v} = 0{\cdot}6$).

Preparation of Methylated Galactan; Hydrolysis, and Separation of Methylated Sugars.—Partially reduced pectic acid (uronic anhydride, 18%; 8 g.) was methylated with methyl sulphate and sodium hydroxide and partially methylated polysaccharide (as sodium salt) was isolated after dialysis. After treatment with Amberlite resin IR-120(H) to remove sodium ions, the acid was converted into the silver salt by neutralisation with silver carbonate. Dry silver salt was dissolved in methyl iodide (150 ml.), and silver oxide (50 g.) was added slowly during 6 hr. to the boiling solution; the mixture afforded methylated polysaccharide (5·2 g.) (Found: OMe, 41·3%). Lithium aluminium hydride (3 g.) in tetrahydrofuran (150 ml.) was added slowly to the methylated polysaccharide (5·2 g.) in boiling tetrahydrofuran (100 ml.) and refluxing was continued for 1 hr. The reduced methylated polysaccharide, after separation from inorganic salts, was methylated twice with methyl iodide and silver oxide to give methylated galactan (3·8 g.), $[\alpha]_D$ +177° ± 1° (*c* 3·0 in H_2O), +158° ± 2° (*c* 3·2 in $CHCl_3$) (Found: OMe, 42·5%).

Methylated galactan (3·5 g.) was refluxed for 5 hr. with methanol (75 ml.) and 2N-hydrochloric acid (75 ml.). Methanol was evaporated under reduced pressure, water was added, and the solution (N with respect to hydrochloric acid) was heated at 100° for 3 hr. The cooled solution was neutralised with silver carbonate, filtered, and concentrated to a syrup (3·12 g.) which was separated on cellulose (75 × 3·9 cm.) by means of light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3) saturated with water as eluant to give four fractions.

Fraction 1. Chromatography of the syrup (759 mg.) showed three components (R_G 1·00, 0·96, and 0·87). A sample was hydrolysed and since the fastest-moving component disappeared

[11] Flood, Hirst, and Jones, *J.*, 1948, 1679.

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with the formation of 2 : 3 : 6-tri-*O*-methylgalactose (R_G 0·73) it is probable that either a methyl glycoside or a polymer of 2 : 3 : 6-tri-*O*-methylgalactose was present. The syrup (750 mg.) was re-hydrolysed with N-hydrochloric acid for 5 hr. and quantitative chromatography of the hydrolysate showed 2 : 3 : 5-tri-*O*-methylarabinose (R_G 0·96; 200 mg.), 2 : 3 : 4 : 6-tetra-*O*-methylgalactose (R_G 0·87; 140 mg.) and 2 : 3 : 6-tri-*O*-methylgalactose (R_G 0·73; 410 mg.). Larger quantities of the sugars were separated on filter sheets with solvent H, and 2 : 3 : 5-tri-*O*-methyl-L-arabinose was characterised by conversion into 2 : 3 : 5-tri-*O*-methyl-L-arabonamide, m. p. and mixed m. p. 137—139°, 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose was characterised as the aniline derivative, m. p. and mixed m. p. 194—196°, and 2 : 3 : 6-tri-*O*-methyl-D-galactose was characterised by conversion into 2 : 3 : 6-tri-*O*-methyl-D-galactonolactone, m. p. and mixed m. p. 97—99°.

Fraction 2. The syrup (778 mg.), $[\alpha]_D$ +82° (*c* 3·6 in H_2O), contained 2 : 3 : 6-tri-*O*-methyl-D-galactose (*ca.* 720 mg.) and 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose (*ca.* 58 mg.) (approximate quantities calculated from the optical rotation). The main component was identified by conversion into 2 : 3 : 6-tri-*O*-methyl-D-galactonolactone, m. p. and mixed m. p. 98—99°.

Fraction 3. The sugar (R_G 0·73; 759 mg.), $[\alpha]_D$ +79·4° (*c* 4·8 in H_2O), was identified as 2 : 3 : 6-tri-*O*-methyl-D-galactose by conversion into 2 : 3 : 6-tri-*O*-methyl-D-galactonolactone, m. p. and mixed m. p. 97—99°.

Fraction 4. The syrup (420 mg.) contained di-*O*-methylgalactose (R_G 0·51) together with small amounts of other sugars (R_G 0·94, 0·85, 0·72, and 0·24). The di-*O*-methylgalactose fraction was separated by chromatography on filter sheets, and chromatography of the sugar mixture in solvent C and of the periodate oxidation products indicated the presence of the 2 : 3-, 2 : 4-, and 2 : 6-dimethyl ether. The presence of 2 : 4-di-*O*-methyl-D-galactose was confirmed by the formation of its aniline derivative, m. p. and mixed m. p. 207—209°.

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811. *Effect of Various Anions on Thickness and Active-oxygen Content of Nickel Oxide Layers formed by Repeated Anodic–Cathodic Cycling; the Specific Effect of Chloride Ions and Its Dependence on the Nature of the Substrate.*

By H. K. EMBABY and A. A. MOUSSA.

The effect of the fluoride, nitrate, perchlorate, and chloride anions on the thickness and active oxygen content of nickel oxide layers formed by repeated anodic–cathodic cycling on nickel and platinum substrates in a bath of a nickel salt was investigated. At concentrations from 10^{-4} to 10^{-1}N the first three ions had no effect, and on both substrates the thickness and active-oxygen content were essentially the same as for layers formed in the original bath alone. On a nickel substrate, chloride ions at or above 0·02N exhibited a specific effect, bringing about, though indirectly, considerable increase in layer thickness, and preventing almost completely the formation of active oxygen. On platinum these ions were ineffective. The specific effect of chloride ions is discussed and the advantage of repeated cycling in furnishing oxide layers of reproducible behaviour during anodic oxidation in 1·0M-sodium hydroxide over that of mere cathodic deposition illustrated.

THAT metals which tend to be passive can be activated by certain anions is well known. These anions are considered[1] somehow to hamper the progression of passivation

[1] Kabanov, Burstein, and Frumkin, *Discuss. Faraday Soc.*, 1947, **1**, 259; Hoar, *Trans. Faraday Soc.*, 1949, **45**, 633.

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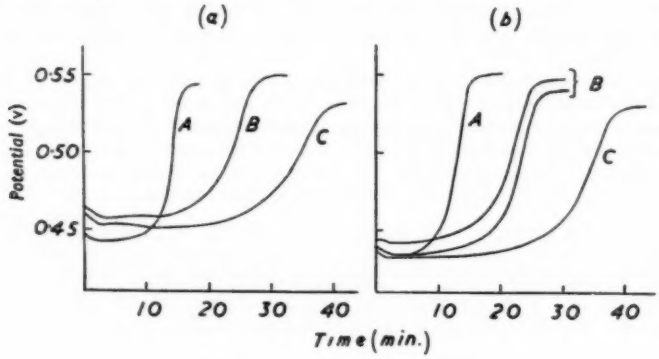
$OH^- \longrightarrow OH + e$ while allowing free anodic dissolution of the metal. However, the effect of such anions on anodic oxidation of a lower oxide when allowed to proceed on substrates of different materials with constant composition on the solution side of the interface has not previously been investigated. The preparation of nickel oxide layers by repeated anodic–cathodic cycling was described recently by Wynne-Jones and his co-workers;[2] with both nickel and platinum as substrates, the formed layer at the end of the last cathodic duration was shown[3] by *X*-rays to be essentially $Ni(OH)_2$, and contained measurable quantities of active oxygen whose presence is undoubtedly pertinent since nickelous hydroxide free from active oxygen can be formed by cathodic deposition under similar conditions.[4]

FIG. 1. *Plot of electrode potential relative to that of a mercury–mercuric oxide electrode during anodic oxidation of layers of nickelous hydroxide deposited during* (*A*) 5 *min.*, (*B*) 10 *min.*, *and* (*C*) 15 *min. on* (*a*) *platinum and* (*b*) *nickel.*



From a bath containing (cf. ref. 3) 0·1N-nickel sulphate, 0·1N-sodium acetate, and 0·001N-sodium hydroxide, nickelous hydroxide was cathodically deposited on nickel and platinum with a current efficiency of almost 100%: $Ni^{++} + 2H_2O + 2e \longrightarrow Ni(OH)_2 + H_2$. Analyses of nickel in the formed layers agreed to within 3—5%; typical amounts of nickel (10^{-6} g.-atom/cm.$^{-2}$) on platinum at a constant current of 2·0 mA/cm.^{2} of apparent area after various periods (min.) were 1·5, 0·9; 3·0, 1·9; 5·0, 2·9; 7·5, 4·4; 10·0, 6·1; 15·0, 9·2. The layers were pale green and did not contain active oxygen. When freshly deposited, then anodically oxidised in 1·0M-sodium hydroxide at 0·5 mA/cm.^{2}, they gave plots as shown in Fig. 1. Before the final resting stage corresponding to evolution of oxygen, each plot shows an arrest of length almost proportional to the layer thickness and, judged by the amount of electricity passed, such as to correspond to the oxidation of bi- to ter-valent nickel. However, it is conspicuous that the curves for layers of the same thickness on the different substrates do not coincide.

These results seem to support Wynne-Jones's suggestion that during repeated cycling oxide layers are formed mainly during the cathodic duration of the current. Oxidation of the deposited layer followed by evolution of oxygen, two processes due to the primary discharge of hydroxyl ions, would then occur during the anodic duration. As it appeared that this discharge might be hindered by the presence of other ions, we did the present work.

Produced by the eleven-cycle scheme[2] at a constant current of 2·0 mA/cm.^{2} the oxide layer obtained on each of nickel and platinum in the original bath appeared dark grey or

[2] Briggs, Jones, and Wynne-Jones, *Trans. Faraday Soc.*, 1955, **51**, 1433.
[3] Briggs and Wynne-Jones, *ibid.*, 1956, **52**, 1272.
[4] Salt, *Discuss. Faraday Soc.*, 1947, **1**, 169.

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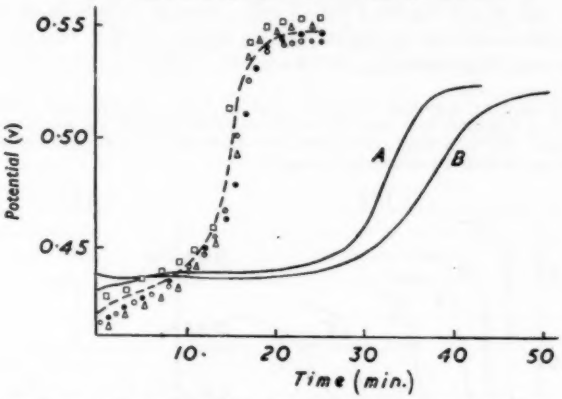
almost black. Its nickel and active-oxygen contents were $3\cdot7$—$3\cdot9 \times 10^{-6}$ and 4—6×10^{-7} g.-atom/cm.^{2} respectively, agreeing satisfactorily with previous results.[2] When oxidised anodically in 1·0M-sodium hydroxide at 0·5 mA/cm.^{2}, the metal gave a plot for such a layer as shown in Fig. 2 (broken line). With the bath made 10^{-4}, 10^{-3}, 10^{-2}, and 10^{-1}N in each of F^-, NO_3^-, ClO_4^-, and Cl^- ions successively by adding the potassium salts, and using a nickel substrate, the first three anions at all concentrations, and chloride ions up to 0·01N, had no effect on appearance, composition, or behaviour during anodic oxidation of the layer formed. At a critical concentration of $2\cdot0 \times 10^{-2}$N, chloride ions brought about a

FIG. 2. *Plot of electrode potential relative to that of a mercury–mercuric oxide electrode during anodic oxidation of layers of nickelous hydroxide.*



The broken line refers to the bath alone, and the symbols ○, ●, and △ to the presence of 0·1N-fluoride, -nitrate, and -perchlorate ions respectively, all on nickel and on platinum. □ refers to 0·1N-chloride ion on platinum, and curves *A* and *B* to 0·02 and 0·04N-chloride ion, respectively, on nickel.

considerable increase in layer thickness. The nickel content increased to about $7\cdot5 \times 10^{-6}$ g.-atom/cm.^{2}, and that of active oxygen decreased to a trace; the layer appeared greyish-green. At 0·04N-Cl^-, the layer formed was not easily visible; its nickel content was only slightly greater, *viz.*, $7\cdot8 \times 10^{-6}$ g.-atom/cm.^{2}, and it contained almost no active oxygen. With platinum no anion was effective, although the layer formed in presence of 0·1N-chloride ion resisted dissolution in dilute sulphuric acid somewhat. Some anodic plots are shown in Fig. 2.

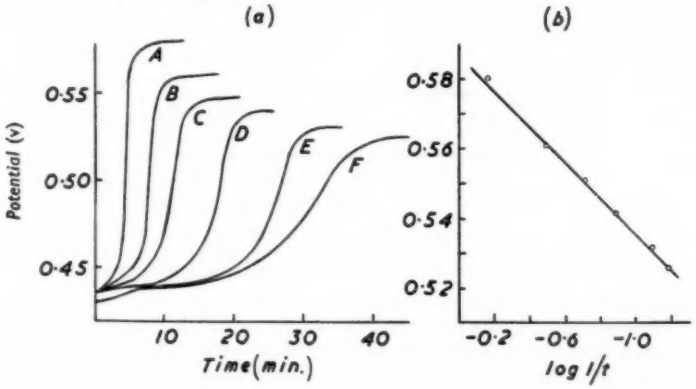
The specific effect of chloride ions in increasing layer thickness on a nickel but not on a platinum substrate, while preventing almost completely the deposition of active oxygen is no doubt significant since it shows that the different processes involved must be intimately related. According to the adsorption theory of Kabanov *et al.*[1] and judged by the behaviour of the various anions at the mercury interface,[5] the effect may be explained by the ready specific adsorption of chloride ions which so increase the field energy in the electrical double layer condenser that the nickel atoms of the substrate are loosened. The activated anodic process $Ni \longrightarrow Ni^{++} + 2e$ then proceeds in preference to the passivating process $OH^- \longrightarrow OH + e$. On a platinum substrate chloride ions up to 0·1N do not hinder the deposition of hydroxyl ions, nor do they on a nickel substrate below a critical concentration of 0·02N. The pH of the bath, with or without added salts, varied between 6·5 and 6·8. At the critical chloride-ion concentration, the ratio Cl^- : OH^- is then roughly 10,000 : 1. The same ratio causes change [6] from preferential water-line

[5] Grahame, *Chem. Rev.*, 1947, **41**, 441; Grahame, Poth, and Cummings, *J. Amer. Chem. Soc.*, 1952, **74**, 4422.
[6] Peers, *Trans. Faraday Soc.*, 1955, **51**, 1748.

attack to general attack on oxide-bearing iron anodes. From our measurements of the differential capacity of mercury in an excess of a supporting electrolyte which did not exhibit specific adsorption and containing both anions, the same ratio caused the pseudo-capacity peaks on the anodic side of the electrocapillary maximum to coincide, thus indicating simultaneous dissolution of mercury as chloride and hydroxide.[7]

The activating effect of the chloride ions seems, however, to bear indirectly on the increase in layer thickness brought about in their presence. In a bath 0·1N with respect to Ni^{++} ions and of pH almost equal to the precipitation pH value of nickelous hydroxide [8] (6·7), the anodically released Ni^{++} ions should be precipitated as $Ni(OH)_2$. If this happened, the hydroxide would be deposited probably some distance from the anode surface. This was supported by the fact that at a polished nickel substrate anodised first in the presence of 0·04N-chloride ions at 2·0 mA/cm.^{2} for 15 min., then in 1·0M-sodium hydroxide at 0·5 mA/cm.^{2}, the oxygen-evolution potential in the latter solution reached, within 3 to 4 minutes from the start of polarisation, 0·594—0·600 v with respect to a mercury–mercuric

FIG. 3. (*a*) *Plot of electrode potential relative to that of a mercury–mercuric oxide electrode during anodic oxidation of nickelous hydroxide layers deposited during* (*A*) 1·5 *min.*, (*B*) 3·0 *min.*, (*C*) 5·0 *min.*, (*D*) 7·5 *min.*, (*E*) 12·0 *min.*, (*F*) 15·0 *min. on nickel.* (*b*) *Oxygen-evolution potential as a function of time of deposition, followed by cycling.*



oxide electrode with no indication of previous separation of nickelous hydroxide on the electrode surface. The stimulating effect of chloride ions may therefore be considered as primarily due to the hindrance of hydroxyl-ion deposition so that the nickelous hydroxide formed during the successive cathodic intervals accumulates. For the eleven-cycle scheme used, the total duration of the cathodic current was 15·0 min., and cathodic deposition yields in this period approximately $9{\cdot}2 \times 10^{-6}$ g.-atom of nickel/cm.^{2}; this agrees quite satisfactorily with that found experimentally for layers obtained on nickel by repeated cycling in presence of chloride ions.

It seems that the main advantage in preparing nickel oxide layers by repeated cycling [2] lies in the co-deposition of active oxygen. That the latter was essential for a well-defined and reproducible behaviour during anodic oxidation in alkali was substantiated as follows. After having been deposited cathodically on nickel, the layer, while still in the bath, was subjected to one cycle only, first anodically then cathodically, at the same current density and for the same period, t, as that of deposition. The formed layer appeared dark grey, and the active-oxygen content varied between 1 and 3×10^{-7} g.-atom/cm.^{2}, independently of thickness. The anodic plots for the so-treated layers in 1·0M-sodium hydroxide are shown in Fig. 3(*a*); the arrest indicating oxidation of bi- to ter-valent nickel occurs sharply

[7] Unpublished results; also Moussa, Sammour, and Ghaly, *J. Phys. Chem.*, 1958, **62**, 1017.
[8] Britton, "Hydrogen Ions," Chapman and Hall, London, vol. 2, 1942, p. 39.

at 0·442 v. Further, the plot of oxygen-evolution potential against log (1/*t*) [Fig. 3(*b*)], is almost straight, indicating that on such layers the relation between oxygen over-potential and current density is logarithmic, and that the effective current density is inversely proportional to the layer thickness as found by Jones and Wynne-Jones with layers formed by repeated cycling.[9]

Experimental

Nickel (Merck) was 99·8% pure. The substrates were in the form of sheets 1 × 2 cm. The nickel sheets were jammed into stiff wire wedges of the same material, and were kept tightly in position by slipping the wires into thick narrow-bored Polythene tubes. The platinum sheets were welded to short platinum wires which were then sealed into soda-glass tubes as usual. Before use, the nickel sheets were polished bright with 3/0 emery paper. The platinum sheets were first boiled in concentrated nitric acid for a few min., washed thoroughly, and then burnt in an alcohol flame. All other materials were " AnalaR."

Oxide layers were formed, cathodically and by repeated cycling, in a Haring cell with a middle compartment of about 80 ml. separated from the side compartments by sintered-glass discs. Platinum spirals served as auxiliary electrodes. The layers were anodically oxidised in a simple Pyrex cell with its lead-in capillary kept as close as possible to the anode surface. Polarisation and potential-measuring circuits were essentially the same as described before.[10] Deposition and polarisation were made at 25° ± 0·1° in an air-bath.

Active oxygen was determined iodometrically.[9] Nickel was determined complexometrically; after the liberated iodine had been titrated the solution was made alkaline with ammonia, then titrated with 10^{-3}M-disodium ethylenediaminetetra-acetate dihydrate solution, with murexide as indicator.[11] The method gave very accurate results and the end-point was quite sharp.

Cairo University, Egypt. [*Received, March 7th,* 1958.]

[9] Jones and Wynne-Jones, *Trans. Faraday Soc.*, 1956, **52**, 1260.
[10] Moussa, Embaby, and Sammour, *J.*, 1958, 2481.
[11] Flaschka, *Mikrochim. Acta*, 1952, **39**, 38.

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812. *A Simple MO–LCAO Method for the Calculation of Charge Distributions in Saturated Organic Molecules.*

By Giuseppe Del Re.

A simple method is presented by which charge distributions can be calculated for saturated molecules. It is checked by use of experimental dipole moments, and its applications and limitations are discussed.

The calculation of charge distributions based on the MO–LCAO theory is useful for the understanding of chemical problems.[1] Unfortunately, so far such calculations have been extensively applied only to the case of π-electrons. We now report an investigation on the possibility of applying this theory, in a very rough approximation, to saturated molecules, intending to calculate charges arising from inductive effects.

The proper meaning of bond charges is, in some respects, a matter of discussion, when one is interested in bonds where overlap and hybridization play an important rôle, because they appear not to be directly correlated with any observed property of molecules. Indeed, theoretical considerations induced Coulson,[2] Mulliken,[3] and others to conclude that dipole moments arise from both bond charges and other effects—core polarization, hybridization, overlap, and lone-pair dipoles. Now it has usually been assumed that the

* In the frame of the simple MO–LCAO theory, if a localized bond is described by an MO of the form $c_\mu\phi_\mu + c_\nu\phi_\nu$, the bond charge is given (see ref. 3) by $Q_{\mu\nu} = c_\nu^2 - c_\mu^2$, and may be considered to represent the net amount of electrons either in excess or in defect on atom μ, to which an equal defect or excess on atom ν corresponds.

[1] *E.g.*, Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 31; Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 285; Orgel, *Trans. Faraday Soc.*, 1942, **38**, 433.
[2] Coulson, *Proc. Roy. Soc.*, 1951, *A*, **207**, 63.
[3] Mulliken, *J. Chem. Phys.*, 1949, **46**, 539.

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total contribution of effects other than that of bond charges to dipole moments is not negligible, but if this is so a direct comparison of calculated charges with dipole moments becomes impossible, especially as the other contributions to dipole moments cannot be exactly calculated because the use of Slater's functions—at least with effective charges corresponding to neutral, non-bonded atoms—is probably not correct [4] and because in many cases the extent to which hybridization takes place is uncertain (*e.g.*, for alkyl halides in connection with quadrupole coupling constants [5]).

In spite of this, which would make it impossible to test results by means of dipole moments, the calculation of charges would be interesting if a reliable set of parameters could be found. Even this is difficult, for many well-known reasons, especially if a simple method is to be applied, but although the situation appears hopeless, especially for polyatomic molecules, we think it worth while to try to apply some simplified calculations by using observed dipole moments both as a source of information about parameters and as a test for calculated charges. The tendency has recently grown to think of hybridization as a general phenomenon, which should be considered as the rule, from which special effects cause deviations.[6] Because of hybridization, lone-pair moments are often produced which, according to many calculations,[7,8] are usually much larger than bond moments, whose polarity may even oppose that of the dipole moment of the whole molecule. Now, one might consider the appearance of atomic moments, if non-bonding electrons are present, as the counterpart of hybridization and overlap moments, which may be thought to correspond roughly to the polarization of, say, atom A, induced by the neighbouring atoms B, C, etc. In other words, the appearance of lone-pair moments might be interpreted as an attempt, on the part of atom A, to restore electrical symmetry around its nucleus. A similar and even more easily acceptable consideration might be applied to conclude that in atoms like carbon, hybridization and overlap moments cancel. In particular, hybridization moments depend only upon the atomic orbitals of each atom used to build the molecular eigenfunctions, and not, at least directly, upon the kinds of bond formed by the atom in question, the only dependence on the nature of the bonds being through the form one gives to the atomic orbitals. We conclude that, in atoms where four tetrahedral equivalent orbitals are used to build the molecular orbitals of four bonds, we get four equal contributions from hybridization moments, which, because of their spatial arrangement, cancel. The same will happen in general, at least approximately, if atomic orbitals slightly different from tetrahedral are assumed.

If such a view were accepted, one might be induced to think that the dipole moment of a whole molecule can be described essentially in terms of bond charges. Naturally, this would leave the general features of the MO–LCAO treatment for bond moments unchanged because, when only one bond is considered, such contributions as hybridization and overlap must be taken into account. There are some indications supporting this tentative view. First, the possibility of using some properly chosen "bond moments" additively to predict moments of saturated compounds, even if approximate, appears very strange in molecules containing lone pairs if the above suggestion does not hold at least to some extent. Secondly, Smith, Magee, Ree, and Eyring [9] applied a semi-classical model to predict inductive effects in paraffin halides in which method it was implicitly assumed that atomic charges, centred on the nuclei, could be defined from which the entire dipole moment arose. Thirdly, Mulliken [3,10] calculated the primary moment of hydrogen

[4] See, *e.g.*, Coulson, *Trans. Faraday Soc.*, 1937, **33**, 1479.
[5] Orville-Thomas, *Quart. Rev.*, 1957, **11**, 162.
[6] *E.g.*, Moffitt, *Proc. Roy. Soc.*, 1950, *A*, **202**, 548; Lennard-Jones and Pople, *ibid.*, p. 155.
[7] *E.g.*, Narasimha Rao, *Trans. Faraday Soc.*, 1957, **53**, 1160.
[8] Cohan and Coulson, *Trans. Faraday Soc.*, 1956, **52**, 1163.
[9] Smith, Magee, Ree, and Eyring, *J. Amer. Chem. Soc.*, 1951, **73**, 2263; 1952, **74**, 229; 1953, **75**, 5183; 1956, **78**, 3922.
[10] See also Benedict, Herman, Moore, and Silverman, *J. Chem. Phys.*, 1957, **26**, 1671.

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chloride which agreed fairly well with the observed value, although if no hybridization was introduced the total moment was radically different from, and indeed opposite to, that observed. Finally, Tomiie [11] has compared *X*-ray data for diformylhydrazine with bond charges which he calculated using σ charges found from Hannay and Smith's formula,[12] which is based on the well-known relation between electronegativities and bond moments used in additive calculations. The good agreement further supports our suggestion.

A careful theoretical investigation, in some simple cases, is possible. In ammonia, treated in the usual manner,[8] there appears to be an extremely high value of the atomic dipole of nitrogen, which is not likely to be preserved in a more elaborate calculation,[13] perhaps because the effective charges of atoms in valence states should be much higher than Slater's values,[4] and the strongly directional field of electrons in hybrid orbitals should considerably modify the spatial symmetry of orbitals in favour of electrical symmetry. A rough SCF calculation carried out by evaluating the potential produced by electrons in each hybrid orbital on the other orbitals led us, in the case of tetrahedral orbitals, to conclude that the radial parts of atomic orbitals, when lone pairs are present, should be modified largely in the same way as if we chose a larger value of Z_{eff} for the lone-pair orbitals than for the bonding orbitals. A method for the study of molecules based on similar considerations was recently suggested.[14]

An attempt to see whether our suggestion is reasonable can be made either by very elaborate theoretical calculations or by less sound rough semi-empirical methods. We chose the latter way because it can provide a general procedure to determine approximate bond charges and is applicable to many molecules, so that results can be compared not only with dipole moments, but with other molecular properties.

Procedure.—The application of the simple MO–LCAO method to the calculation of bond charges implies, at least in principle, the solution of the secular equation which, for a localized bond between atoms μ and ν, is:

$$\begin{vmatrix} H_{\mu\mu} - E & H_{\mu\nu} - ES_{\mu\nu} \\ H_{\mu\nu} - ES_{\mu\nu} & H_{\nu\nu} - E \end{vmatrix} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

In order to solve this equation, the values of four parameters, $H_{\mu\mu}$, $H_{\nu\nu}$, $H_{\mu\nu}$, and $S_{\mu\nu}$ are needed. Apart from $S_{\mu\nu}$, which is often neglected, and at any rate is unimportant in our connection, the nature of the simple MO–LCAO method requires that such parameters be evaluated empirically on the basis of the nature of the atoms involved in the bonds and of their surroundings. If, for each bond in a molecule, we apply eqn. (1), we must consequently vary our parameters not only according to the type of bond but also according to the structure of the rest of the molecule. Our procedure was very simple: we started from the usual positions:

$$\begin{aligned} H_{\mu\mu} &= \alpha + \delta_\mu\beta \\ H_{\nu\nu} &= \alpha + \delta_\nu\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2) \\ H_{\mu\nu} &= \varepsilon_{\mu\nu}\beta \end{aligned}$$

with α and β two basic parameters whose values need not be known. We assumed that, to a first approximation $\varepsilon_{\mu\nu}$ was independent of the surroundings, while δ_μ and δ_ν were influenced only by atoms directly bound to μ and ν respectively. Consequently, we assumed that a correct expression for, say, δ_μ should be:

$$\delta_\mu = \delta_\mu^\circ + \sum_{\lambda \text{ adj. to } \mu} \gamma_{\mu(\lambda)}\delta_\lambda \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where δ_μ° and $\gamma_{\mu(\lambda)}$ are two suitable empirical parameters, one depending only upon the nature of atom μ, the other upon atom μ and each adjacent atom λ. Eqn. (3) is one of

[11] Tomiie, unpublished work.
[12] Hannay and Smith, *J. Amer. Chem. Soc.*, 1946, **68**, 171.
[13] Hamilton, *J. Chem. Phys.*, 1957, **26**, 435.
[14] Arai, *J. Chem. Phys.*, 1957, **26**, 435.

the n equations giving the δ's for the n atoms on the molecule under study. The whole set of these equations gives a linear system in the unknowns δ_μ, δ_ν, ..., which can easily be solved. In order to calculate charges, one can either proceed in the usual manner or (usually a very good approximation) use the equation [3]

$$Q_{\mu\nu} = (\delta_\nu - \delta_\mu)/2\varepsilon_{\mu\nu} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Provided that δ's, γ's, and ε's are known, eqn. (4) gives the bond charges, whose sum over all bonds formed by an atom gives the total apparent charge of that atom in the molecule.

For example, let us suppose that $\delta_H^\circ = 0{\cdot}00$, $\delta_C^\circ = 0{\cdot}07$, $\delta_N^\circ = 0{\cdot}24$; $\varepsilon_{CH} = 1{\cdot}00$, $\varepsilon_{CN} = 1{\cdot}00$, $\varepsilon_{NH} = 0{\cdot}45$; $\gamma_{H(C)} = \gamma_{H(N)} = 0{\cdot}4$; $\gamma_{C(C)} = \gamma_{C(N)} = \gamma_{N(C)} = 0{\cdot}1$; $\gamma_{C(H)} = \gamma_{N(H)} = 0{\cdot}3$; and let us calculate the charge distribution of dimethylamine, $(CH_3)_2NH$. To find the δ's we must solve the system:

$$\begin{aligned}
\delta_{H_1} &= \delta_H^\circ + \gamma_{H(C)}\delta_C \\
\delta_C &= \delta_C^\circ + 3\gamma_{C(H)}\delta_{H_1} + \gamma_{C(N)}\delta_N \\
\delta_N &= \delta_N^\circ + 2\gamma_{N(C)}\delta_C + \gamma_{N(H)}\delta_{H_2} \\
\delta_{H_2} &= \delta_H^\circ + \gamma_{H(N)}\delta_N
\end{aligned}$$

where H_1 is a hydrogen atom of the methyl group and H_2 that of the amino-group. There should really be 10 equations, but the six hydrogen atoms of the methyl groups are equivalent, as are the two carbon atoms. Substitution of the numerical values leads to:

$$\delta_{H_1} = 0{\cdot}063; \quad \delta_C = 0{\cdot}158; \quad \delta_N = 0{\cdot}309; \quad \delta_{H_2} = 0{\cdot}123$$

By use of eqn. (4) one immediately deduces that:

$$Q_{HC} = 0{\cdot}047; \quad Q_{CN} = 0{\cdot}075; \quad Q_{HN} = 0{\cdot}206$$

Correspondingly, the charges of the atoms are:

$$Q_{H_1} = 0{\cdot}047; \quad Q_C = -0{\cdot}066; \quad Q_N = -0{\cdot}356; \quad Q_{H_2} = 0{\cdot}206$$

where, for instance,

$$Q_C = -3Q_{HC} + Q_{CN}$$

From bond charges bond moments can also be deduced, by multiplying them by the experimental bond distances. A suitable choice of the bond angles very easily gives the total expected moment by vectorial addition. In our example, if all angles are taken as tetrahedral, the calculated moment is 0·9 D, while the experimental value is 1·0 D.

Before describing how parameters were chosen, and some results, we suggest one possible theoretical interpretation of our assumptions. Consider a monoelectronic bicentric LCAO–MO of the form $C_\mu\psi_\mu + C_\nu\psi_\nu$, with ψ_μ and ψ_ν appropriate atomic orbitals. Let the total Hamiltonian be of the form:

$$H = H_\mu - \sum_{\lambda \neq \mu} \frac{Z_\lambda}{r_\lambda} = H_\nu - \sum_{\lambda \neq \nu} \frac{Z_\lambda}{r_\lambda} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

the Z_λ's being appropriate "effective charges" and H_μ and H_ν the Hamiltonians for atoms μ and ν. The matrix elements of H will be:

$$\begin{aligned}
H_{\mu\mu} &= E_\mu - \sum_{\lambda \neq \mu} \int \frac{Z_\lambda \psi_\mu^2}{r_\lambda} \, d\nu \\
H_{\nu\nu} &= E_\nu - \sum_{\lambda \neq \nu} \int \frac{Z_\lambda \psi_\nu^2}{r_\lambda} \, d\nu
\end{aligned} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$H_{\mu\nu} = \beta_{\mu\nu} - \sum_{\lambda \neq \mu, \nu} \int \frac{Z_\lambda \psi_\mu \psi_\nu}{r_\lambda} \, d\nu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

with $$E_\mu = \int \psi_\mu H_\mu \psi_\mu d\nu, \; E_\nu = \int \psi_\nu H_\nu \psi_\nu d\nu, \; \beta_{\mu\nu} = \int \psi_\mu \left(H_\mu - \frac{Z_\nu}{r_\nu} \right) \psi_\nu d\nu$$

Eqns. (6) and (7) are valid only for the monoelectronic case, and they depend strongly upon the actual form of ψ_μ and ψ_ν, and, in a second-order approximation, upon the ψ_λ's. However, we can suppose that monoelectronic orbitals are correct, provided we do not take in explicitly the forms of the atomic orbitals, do not evaluate E and β on the basis of free-atom properties, and consider the Z's as involving also the contributions to the potential energy of electrons other than the one we are considering. Now, eqns. (6) and (7) can be written as:

$$H_{\mu\mu} = \alpha + \delta_\mu{}^\circ\beta - \sum_\lambda I_{\mu(\lambda)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

$$H_{\mu\nu} = \beta_{\mu\nu} - \sum_\lambda I_{\mu\nu(\lambda)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

with $I_{\mu(\lambda)}$ and $I_{\mu\nu(\lambda)}$ the integrals which appear explicitly in eqns. (6) and (7). Thus, our previous assumptions are equivalent to putting (*a*) $I_{\mu(\lambda)} = -\gamma_{\mu(\lambda)}\delta_\lambda$ for μ and λ adjacent, (*b*) $I_{\mu(\lambda)} = 0$ for μ, λ not adjacent, and (*c*) $I_{\mu\nu(\lambda)} = 0$. Therefore, let us consider $I_{\mu(\lambda)}$ and $I_{\mu\nu(\lambda)}$, and assume that Z_λ does not depend upon whether atom λ forms the bond we are interested in, but only depends upon whether atom λ is adjacent to atom μ, whose coulombian integral we are considering. (This assumption amounts only to introducing an " average potential " produced by atom λ on atom μ.) Let us assume, too, that Z_λ is centred on the nucleus of atom λ. A rough approximation, obtained by considering the orbital ψ_μ as a finite sphere centred on the nucleus of atom μ, gives:

$$\int \frac{Z_\lambda \psi_\mu{}^2}{r_\lambda} \mathrm{d}v = \frac{Z_\lambda}{R_{\mu\lambda}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

Similarly, the mixed integral of eqn. (7) might be approximated as:

$$\int \frac{Z_\lambda \psi_\mu \psi_\nu}{r_\lambda} \mathrm{d}v = \frac{2Z_\lambda S_{\mu\nu}}{R_{\mu\lambda} + R_{\nu\mu}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

In the case of eqn. (11) both Z_λ and $S_{\mu\nu}$ may be supposed to be small enough to make it possible to neglect the mixed integral $I_{\mu\nu(\lambda)}$. This corresponds to the assumption that $\delta_{\mu\nu}$ should not be much influenced by the surroundings of the bond under study. As to eqn. (10), it is far too rough to be used directly, especially if hybrid orbitals are involved. However, it shows that $I_{\mu(\lambda)}$ should depend principally upon the apparent charge of atom λ at a distance $R_{\mu\lambda}$, and upon the reciprocal of the distance itself, so that it should rapidly decrease when $R_{\mu\lambda}$ increases. This justifies approximation (*b*). As to (*a*), eqn. (10) suggests that $I_{\mu(\lambda)}$ should be apt to be split into two factors, one of which should depend only upon atom μ while the other should represent something like a " polarizability " of atom μ on the part of atom λ.

Determination of Parameters.—In order to determine parameters, an obvious procedure might be to introduce eqn. (4) into the equations giving the dipole moments of a properly chosen set of molecules. However, this would be useless because there are not enough molecules for which dipole moments corresponding to definite conformations are known to allow, after use of some of them to determine parameters, a check of the calculated charges by use of the rest. This is because in most saturated compounds the possibility of hindered internal rotation makes their dipole moments uncertain in connection with our problem. Therefore, we culled all possible sources of information for values of the parameters, a procedure which also gives a sounder foundation to our calculations.

In the determination of the values of δ° we started from electronegativities (x), with the obvious equation:

$$\delta_\mu{}^\circ = k(x_\mu - x_\mathrm{H})/x_\mathrm{H} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

If this equation were used as such, k would obviously be the only parameter determinable from dipole moments. However, δ, and not δ°, should be directly correlated with electronegativities, so that, especially in the case of univalent atoms to which large values of γ correspond, some minor changes, after determination of k, were found necessary. k was calculated simply by adjusting ϵ_{CH} to unity.

The next step was to chose values for γ. For these, we had only a clue from the parameters used for π-systems: Pauling and Wheland had, indeed, suggested that, for the effect of hetero-atoms on carbon, a value of 0·1 for the quantity corresponding to our γ should be used.[15] Therefore we assumed that the γ's should have that order of magnitude, and proceeded as follows. We considered the cases of CH_3Cl and $(CH_3)_3CCl$, and set down the corresponding sets of equations (5). We imposed the condition that $\delta_{Cl} - \delta_C$ in the latter should be larger than that in the former, because of the known order of inductive effects of the methyl and the *tert.*-butyl group.[16] This led us to conclude that, approximately, the two conditions to be fulfilled were:

$$\gamma_{H(C)}\gamma_{C(H)} > \gamma_{C(C)}\,; \quad \gamma_{C(Cl)}/\gamma_{Cl(C)} \gg \delta_C^\circ/\delta_{Cl}^\circ$$

Consequently, we assumed $\gamma_{C(C)} = 0{\cdot}1$, $\gamma_{C(H)} = 0{\cdot}3$, and $\gamma_{H(C)} = 0{\cdot}4$. For $\gamma_{C(Cl)}$ and $\gamma_{Cl(C)}$ we chose respectively 0·2 and 0·4 on the basis of the probable marked interaction between chlorine and carbon, and checked those values by calculation of dipole moments of some simple molecules. Values of $\varepsilon_{\mu\mu}$, initially chosen on the basis of dissociation energies, were then modified, in a few cases very considerably, by comparison of calculated with observed moments.

In order not to use new parameters, and in spite of the fact that $I_{\mu(\lambda)}$ depends on $R_{\mu\lambda}$, which varies for different couples of atoms, we assumed that for atoms of the same rows γ should be the same, *e.g.*, $\gamma_{C(C)} = \gamma_{C(N)} = \gamma_{N(C)} = \gamma_{N(O)}$, etc.; $\gamma_{C(H)} = \gamma_{N(H)}$, etc. The molecules used for the determination of parameters were H_2O, $CH_3{\cdot}OH$, $CH_3{\cdot}Cl$, $CHCl_3$, CH_3F, NH_3, $CH_3{\cdot}NH_2$. In Table 1 the final choice of parameters is given.

TABLE 1. *Parameters used.*

Bond	C–H	C–C	C–N	C–O	C–F	N–H	O–H	C–Cl
ε_{AB}	1·00	1·00	1·00	0·95	0·85	0·45	0·45	0·65
$\gamma_{A(B)}$	0·3	0·1	0·1	0·1	0·1	0·3	0·3	0·2
$\gamma_{B(A)}$	0·4	0·1	0·1	0·1	0·1	0·4	0·4	0·4
δ_A°	0·07	0·07	0·07	0·07	0·07	0·24	0·40	0·07
δ_B°	0·00	0·07	0·24	0·40	0·57	0·00	0·00	0·35

The following must be noted; (1) The results, particularly in the case of dipole moments, are very sensitive both to the second decimal place of the γ's and ε's, and to the third decimal place of the δ°'s. However, given the roughness of our assumptions, and in view of our present purpose to elaborate and test a method, we approximated the values of the parameters to 0·1, 0·05, and 0·01 respectively. (2) There is a degree of arbitrariness in our choice of parameters. However, they are so inter-related that change of one involves change of all so that their "self-consistency" limits very strongly the arbitrariness in question. Moreover, given the fair agreement of calculated moments with experimental data, such a "self-consistency" strongly supports the reliability of our present method.

Results.—Some results for appropriate charge distributions are given in Table 2. In Tables 3, 4, and 5, some comparisons are illustrated. Table 6 gives some results about energies.

Charges. It is important that charges should agree with the variation of inductive effects deduced, from many properties of molecules, for groups such as alkyl. In general, our calculated charges do agree with the usually accepted variation of inductive effects. However, the definition of inductive effects is based not only on physical properties of molecules, but also on their chemical behaviour, so that dipole moments do not always agree with their supposed variation. In those cases also our calculated charges do not agree: *e.g.*, the increment of charge on the nitrogen atom is reproduced, even if weakly, in passing from methyl- to ethyl-amine, but that calculated for passage from methyl- to dimethyl-amine does not correspond to the variation in basicity.

[15] Wheland and Pauling, *J. Amer. Chem. Soc.*, 1935, **57**, 2086.
[16] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953.

The latter case will be considered when we speak of energies. Except for these special cases, the well-known [16] sequence of inductive effects $CH_3^- < CH_3{\cdot}CH_2^- < (CH_3)_2CH^- < (CH_3)_3C^-$ is perfectly reproduced, and this shows that eqn. (3), which we contrived to satisfy the relation $CH_3^- < (CH_3)_3C^-$, is at least satisfactory as an interpolation formula: this is important in connection with the feature of the present method which more strictly

TABLE 2. *Atomic charges.*

Compound	1	2	3	4	5	6	7
$H_3C{\cdot}Cl$	+0·075	−0·058	−0·167				
$H_3C{\cdot}CH_2Cl$	+0·043	−0·089	+0·001	+0·068	−0·177		
$H C)_2CHCl$	+0·043	−0·093	+0·053	+0·063	−0·186		
$C)_3CCl$	+0·042	−0·097	+0·106	−0·193			
$CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CHCl$	−0·071	+0·038	−0·051	+0·041	+0·037	+0·063	−0·172
$(H_3C)_2CCl_2$	+0·046	−0·077	+0·174	−0·148			
H_3CCl_2	+0·105	+0·024	−0·117				
$HC{\cdot}Cl_3$	+0·131	+0·056	−0·063				
$H_3C{\cdot}CCl_3$	+0·051	−0·043	+0·181	−0·097			
NH_3	−0·750	+0·250					
$H_3C{\cdot}NH_2$	+0·049	−0·058	−0·537	+0·225			
$H_3C{\cdot}CH_2{\cdot}NH_2$	+0·040	−0·110	−0·011	+0·046	−0·539	+0·224	
$(H_3C)_2NH$	+0·047	−0·066	−0·356	+0·206			
$(H_3C)_3N$	+0·041	−0·058	−0·198				
H_2O	+0·351	−0·702					
$H_3C{\cdot}OH$	+0·055	−0·011	−0·472	+0·318			
$H_3C{\cdot}CH_2{\cdot}OH$	+0·041	−0·105	+0·039	+0·052	−0·476	+0·317	
$(H_3C)_3C{\cdot}OH$	+0·040	−0·109	+0·131	−0·480	+0·314		
$(H_3C)_2O$	+0·053	−0·023	−0·272				
$(H_3C{\cdot}CH_2)_2O$	+0·040	−0·105	+0·024	+0·050	−0·280		
$CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}O$	−0·060	+0·039	+0·023	+0·050	−0·282		
$O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CH{\cdot}CH_3$	+0·120	+0·051	−0·413	+0·263	+0·070	−0·071	+0·040
$H_3C{\cdot}F$	+0·060	+0·049	−0·229				
H_2CF_2	+0·075	+0·256	−0·203				
HCF_3	+0·085	+0·470	−0·185				

relates to inductive effects. The fact that, in general, hydrogen does not show an inductive effect feebler than alkyl groups can be interpreted similarly to our interpretation of the anomaly of amines.

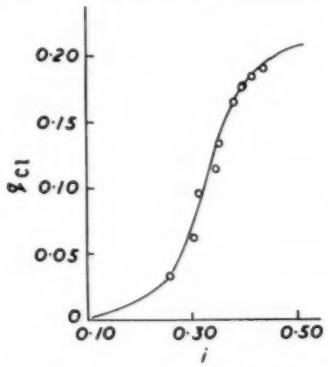
Quadrupole coupling constants. A comparison of calculated charges with quadrupole coupling constants would be valuable. Unfortunately, only a few substances were studied;

most of them were studied in the solid state; and the meaning [5] of eQq^{mol} is still uncertain. However, a qualitative comparison can be made for alkyl halides (Table 3 and Figure). No meaning should be inferred from the shape of the curve, as the values relate [17] to

TABLE 3. *Comparison of calculated charges (q) with the function* $i = 1 - (eQq^{mol}/2eQq^{atom})$ *for* ^{35}Cl.

Compound.	q	i	Compound	q	i	Compound	q	i
CCl_4	0·034	0·256	$CH_2{\cdot}CHCl_2$	0·135	0·350	$CH_3{\cdot}CH_2{\cdot}CH_2Cl$	0·178	0·395
$CHCl_3$	0·063	0·300	$(CH_3)_2CCl_2$	0·148	—	$(CH_3)_2CHCl$	0·186	0·414
$CH_3{\cdot}CCl_3$	0·097	0·307	CH_3Cl	0·167	0·378	$(CH_3)_2CCl$	0·193	0·434
CH_2Cl_2	0·117	0·341	$CH_3{\cdot}CH_2Cl$	0·177	0·400			

Values are from Gordy, Smith, and Trambarulo, ref. 17.



solids where molecules interact in a way dependent on their shape and packing, but charges and quadrupole coupling constants do appear to be correlated.

Dipole moments. Our aim was to test charges by comparison with observed electric dipole moments. In Table 4 we list molecules for which we calculated dipole moments, and it must be noted that: (1) Starred (*) molecules were used for the determination of

TABLE 4. *Observed (a) and calculated (b) dipole moments.*

	(a)	(b)		(a)	(b)		(a)	(b)
$*NH_3$	1·5	1·3	$*H_2O$	1·8	1·9	$*CH_3{\cdot}Cl$	1·9	1·8
$*CH_3{\cdot}NH_2$	1·3	1·3	$*CH_3{\cdot}OH$	1·7	1·7	CH_2Cl_2	1·6	1·7
$CH_3{\cdot}CH_2{\cdot}NH_2$	0·99	0·85— 1·34	$CH_3{\cdot}CH_2{\cdot}OH$	1·7	1·7	$*CHCl_3$	1·0	1·2
			$(CH_3)_3C{\cdot}OH$	1·7	1·7	$(CH_3)_2CCl$	2·1	2·1
$(CH_3)_2NH$	1·0	0·9	$(CH_3)_2O$	1·3	1·4	$CH_3{\cdot}CCl_3$	1·8	1·9
$(CH_3)_3N$	0·6	0·6	$CH_2{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2$	1·7	1·6	$CH_2{\cdot}CH_2{\cdot}CHCl{\cdot}CH_2{\cdot}CH_2$	2·1	1·8
$(CH_3)_2C{\cdot}NH_2$	1·4	0·9	$CH_2{\cdot}O{\cdot}CH(CH_3){\cdot}O{\cdot}CH_2$	1·2	0·8	$*CHF_3$	1·6	1·6
						CH_2F_2	1·9	2·0

Values are from Landolt–Börnstein " Tabellen," Berlin, 1950, and Gordy, *et al.*, ref. 17.

parameters; we did not try to make their calculated and observed dipole moments coincide perfectly because of the approximations used to obtain values for the parameters. (2) The dipole moments are given only to the first decimal place, because that is the limit of reliability of the approximation. (3) For high-molecular weight compounds, which cannot be vaporized, results may be influenced by association in solvents and by the neglect or arbitrary introduction of atomic polarizations—the large difference for *tert.*-butylamine is probably due to measurements' being made on solutions: ethylamine behaves similarly in that its dipole moment from gas measurements is 0·9 D, from solutions 1·3 D.

[17] Gordy, Smith, and Trambarulo, " Microwave Spectroscopy," Wiley, New York, 1953.

However, the overall agreement is fair, especially in view of the sensitivity of dipole moments to parameters. It is encouraging that the method still works, even if approximately, for compounds more complex than simple alcohols (*e.g.*, tetrahydrofuran and 2-methyldioxolan, for which the calculations were made by assuming a regular pentagonal ring and tetrahedral angles for carbon orbitals external to it).

Bond moments. According to our calculations, bond moments are often very variable because we tried to take inductive effects into account. However, the mean values of bond moments appear not to be very different from additive bond moment values, as shown in Table 5. This may be thought to represent the connecting link between usual additive calculations of dipole moments and ours.

TABLE 5. *Bond moments.*

(*a*)	(*b*)	(*a*)	(*b*)
μ(CH) from 0·20 to 0·28 D	0·3 D	μ(CO) from 0·93 to 1·14 D	0·86 D
μ(CN) from 0·47 to 0·62 D	0·45 D [a]	μ(OH) from 1·44 to 1·60 D	1·53 D
μ(NH) from 1·21 to 1·08 D	1·31 D	μ(CCl) from 0·83 to 1·65 D	1·56 D

(*a*) From our calculations. (*b*) Bond moments for vectorial addition, as given by Sutton in Braude and Nachod, " Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955, except the starred value, taken from Pullman and Pullman, " Les Théories électroniques de la Chimie Organique," Masson et Cie, Paris, 1952.

Energies. In such simplified calculations, we cannot expect to be able to calculate energies. However, some considerations are possible, which are important in that they allow a clearer insight into the meaning of bond charges as calculated by us. Formally, energies are given by

$$E_{\mu\nu} = 2\alpha + [\delta_\mu + \delta_\nu + \varepsilon_{\mu\nu}\sqrt{(1 + Q_{\mu\nu}^2)}]\beta = E_{\text{rep}} \quad . \quad . \quad . \quad (13)$$

where we neglected overlap because, in comparisons, it is not very important. E_{rep} represents the repulsion energy between the cores of atoms, which was not included in our Hamiltonian.

To show the use of eqn. (6), we consider, as an example, amines and their conjugated acids. We chose this because the basicities of amines do not agree with the order in which our charges decrease: indeed, it has been assumed that the electron-repelling nature of the CH_3^- group increases the charge of nitrogen in amines from ammonia through to trimethylamine, and this has been given as an explanation of the basicities, with an exception for trimethylamine itself, which is much less basic than expected.[18] However, a different explanation is as follows. Consider the reaction $NH_3 + H^+ \rightleftharpoons NR_3H^+$, and let us try to calculate the energy variation ΔE for it from eqn. (13). Let us assume that the γ's are the same for bonds formed by N^+ as for bonds formed by N; that $\delta_{N^+}{}^\circ = 0{\cdot}31$ because of the increase in electronegativity in passing from N to N^+, and that $\varepsilon_{N^+X} = 1{\cdot}33\varepsilon_{NX}$ because ε_{NH} is much smaller than ε_{CH}, to whose value ε_{N^+H} should presumably approach. Such a choice is largely arbitrary but is useful to show that there is at least one set of parameters which leads to an inversion of the order of ΔE's with

TABLE 6. *Dissociation constants of amines.*

$E = E(NR_3H^+) - E(NR_3) - E(H^+) - \Delta E_{\text{rep}}$ [a].

Amine	$\Delta E/\beta$	$pK_b^{25°}$ [b]
NH_3	3·38	4·75
$CH_3{\cdot}NH_2$	3·52	3·37
$(CH_3)_2NH$	3·72	3·22
$(CH_3)_3N$	4·11	4·20

[a] ΔE_{rep} represents the difference between the core repulsion energies of NR_3H^+ and NR_3. [b] From L. F. Fieser and M. Fieser, " Organic Chemistry, " Reinhold, New York, 1957.

respect to charges of nitrogen for mono-, di-, and tri-methylamine. We thus get Table 6 in which, though repulsion energies are not included, the variations of basicities are correctly

[18] Brown, Bartolomey, and Taylor, *J. Amer. Chem. Soc.*, 1944, **66**, 435.

reproduced, except for that of trimethylamine, whose behaviour remains mysterious although its experimental pK_b might correspond to a particularly high repulsion energy.

The preceding calculation is only meant to present an example relating to the possibility of comparing calculated charges with what is usually called " inductive effects," especially when reactivity is concerned.

Discussion.—This work was not intended to provide a final choice of parameters or the best method (even among uncomplicated, quick ones) for the calculation of molecular properties. Some possibly useful aspects and properties were overlooked because we wished only to see whether a simple MO–LCAO method was usable in connection with saturated systems, especially with respect to dipole moments as a check, these, apart from bond lengths and angles, being the only reliable and extensive data upon which to base such a calculation. The charges obtained have the properties required of real charges, and have some right to be considered as such: they give correct dipole moments, correspond to inductive effects, are clearly correlated with quadrupole coupling constants, and the parameters used to calculate them are probably useful to calculate energies, provided one considers only a set of very similar molecules. Therefore whatever the real meaning of the charges calculated, we may reasonably expect that they are somehow connected with other molecular properties. If so, they may be used to compare molecules, and perhaps find for molecular properties interpretations hitherto overlooked because of the lack of a general method for treating saturated systems.

The author thanks Professor H. C. Longuet-Higgins, who discussed with him the ideas in this paper.

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813. *The Synthesis of Flavan-2 : 3-diols (Dihydro-α : 2-dihydroxychalcones).*

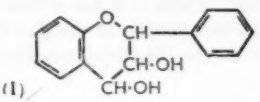
By J. W. GRAMSHAW, A. W. JOHNSON, and T. J. KING.

The products of reduction of luteolinidin and apigeninidin chlorides by lithium aluminium hydride are shown to be flav-2-enes. Hydroxylation of 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene yields a flavan-2 : 3-diol which exists almost entirely as the open-chain tautomer, a dihydro-α : 2-dihydroxychalcone. Treatment of this diol with acid yields cyanidin chloride tetramethyl ether which has been synthesised by an independent route.

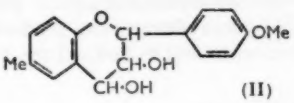
MOST of the *leuco*anthocyanins of known structure are derivatives of flavan-3 : 4-diol (I) and the chemistry of these substances is summarised in recent reviews.[1] Nearly all the syntheses of flavan-3 : 4-diols reported so far have involved the reduction of either a flavonol [2,3,4] or a flavanonol [5,6,7,8] but the syntheses are complicated by the existence of four racemic forms resulting from asymmetric centres at positions 2, 3, and 4. Thus two racemates of 3′ : 4′ : 7 : 8-tetramethoxyflavan-3 : 4-diol were obtained by reduction of the corresponding flavanonol with lithium aluminium hydride and hydrogenation over a platinum catalyst respectively,[6] and each differed from the racemate, the (—)-form of which was identical with tetra-*O*-methylmelacacidin, prepared by hydrogenation of the

[1] Swain and Bate-Smith, " The Chemistry of Vegetable Tannins," Soc. Leather Trades Chemists, Croydon, 1956, p. 109; King, *Sci. Proc. Royal Dublin Soc.*, 1955, **27**, 87.
[2] Mozingo and Adkins, *J. Amer. Chem. Soc.*, 1938, **60**, 669.
[3] Bauer, Birch, and Hillis, *Chem. and Ind.*, 1954, 757.
[4] King and Clark-Lewis, *J.*, 1955, 3384.
[5] Swain, *Chem. and Ind.*, 1954, 1144; Freudenberg and Roux, *Naturwiss.*, 1954, **41**, 450.
[6] Joshi and Kulkarni, *Chem. and Ind.*, 1954, 1421, 1456; 1956, 124.
[7] Bognar and Rakosi, *ibid.*, p. 188.
[8] Keppler, *J.*, 1957, 2721.

corresponding flavonol.[4] Joshi and Kulkarni [6] have also synthesised three of the four racemates (II).



(I)



(II)

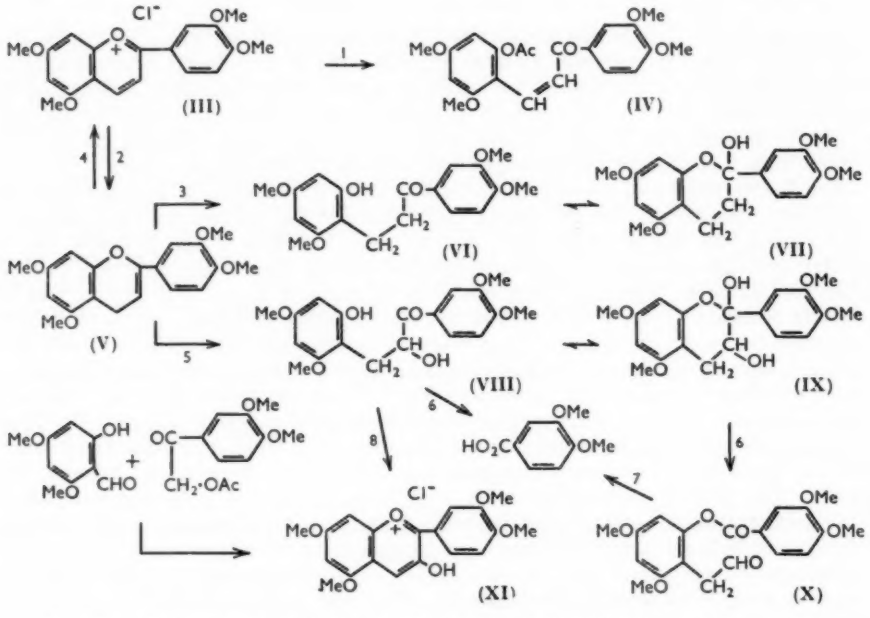
Although some speculations were made concerning the conformations of the heterocyclic-ring substituents, generalisations on the orientations of hydroxyl groups produced by the reductions of cyclic ketones by different methods were somewhat complicated by the observation [7] that the same isomer (I) is produced by reduction of flavanonol with lithium aluminium hydride and by hydrogenation over platinum, although the product differed from that obtained by hydrogenation of flavonol over copper oxide.[2]

The hydroxylation of flav-3-enes seemed to offer an alternative and stereospecific approach to the flavan-3 : 4-diol system and a study of the reaction was undertaken in order to augment the previous views on the stereochemistry of the products and to correlate the conformations of the *leuco*anthocyanins with those of the catechins.[9] Flav-3-enes containing 3-oxygenated substituents were claimed by Karrer and Seyhan [10] as the products obtained from the reduction of the corresponding flavylium salts with lithium aluminium hydride, although in a later study of the reaction [11] it was pointed out that flav-2-ene structures were not excluded for the products. On the other hand flav-2-enes can be obtained by dehydration of *epi*catechins [12,13] and other methods,[14] the structures being assigned on the basis of the method of preparation and chemical properties.[15] Thus, although a dihydro-2-hydroxychalcone was obtained after hydrolysis with dilute acetic acid, the possibility of prototropic rearrangement of the flav-3-ene to the 2-isomer was ignored. We have prepared luteolinidin tetramethyl ether [16] (III) by condensation of 3 : 4-dimethoxyphenyl ethynyl ketone with phloroglucinol dimethyl ether following Johnson and Melhuish's method,[17] and have confirmed the identity of the product by the preparation of derivatives and by ring fission under acetylating conditions whereby 2-acetoxy-4 : 6 : 3′ : 4′-tetramethoxychalcone (IV) was obtained. Reduction of the flavylium chloride (III) with lithium aluminium hydride gave the flav-2-ene (V), the formulation of which is based upon the presence of a free methylene group in the molecule as determined by the measurement of the nuclear magnetic resonance spectrum. We are very grateful to Dr. N. Sheppard who performed this experiment. In a similar series of transformations, condensation of phloroglucinol dimethyl ether and ethynyl *p*-methoxyphenyl ketone gave apigeninidin chloride, which by reduction with lithium aluminium hydride formed 5 : 7 : 4′-trimethoxyflav-2-ene. The flav-2-ene (V) has been prepared previously by Freudenberg and his co-workers [12] by the action of hydrazine on the toluene-*p*-sulphonate of 5 : 7 : 3′ : 4′-tetramethyl*epi*catechin, and acid hydrolysis of (V) gave the dihydrochalcone (VI), tautomeric with the 2-hydroxyflavan (VII). By analogy with the Δ^2-structure of the flavene (V) it is probable that the 3-methoxyflavenes prepared by Karrer and Seyhan [10] are also Δ^2-compounds.

Thus our original objective, the preparation of 3 : 4-dihydroxyflavans, was not possible by this approach but we have been able to utilise the flav-2-ene (V) to prepare and examine

[9] Whalley, "The Chemistry of Vegetable Tannins," Soc. Leather Trades Chemists, Croydon, 1956, p. 109; Birch, Clark-Lewis, and Robertson, *J.*, 1957, 3586.
[10] Karrer and Seyhan, *Helv. Chim. Acta*, 1950, **33**, 2209.
[11] Freudenberg and Weinges, *Annalen*, 1954, **590**, 140.
[12] Freudenberg, Fikentscher, and Harder, *ibid.*, 1925, **441**, 157.
[13] King, Clark-Lewis, and Forbes, *J.*, 1955, 2948.
[14] Shah, Kulkarni, and Joshi, *J. Sci. Ind. Res., India*, 1954, **13**, *B*, 186; Shriner, "The Roger Adams Symposium," John Wiley and Sons, Inc., New York, 1955, p. 103.
[15] Freudenberg *et al.*, *Annalen*, 1925, **442**, 309; 1926, **446**, 87.
[16] Pratt, Robinson, and Williams, *J.*, 1924, **125**, 199.
[17] Johnson and Melhuish, *J.*, 1947, 346.

the properties of a compound of the isomeric 2 : 3-dihydroxyflavan structure. Such compounds are as yet unknown although Karrer and Fatzer [18] suggested that they might cyclise readily to benzoylcoumarans, a prediction which we have not substantiated. Like all simple 2-hydroxyflavans, the product of hydroxylation of the flav-2-ene exhibited ring-chain tautomerism and in fact existed largely as the dihydro-2 : α-dihydroxychalcone

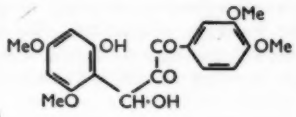


Reagents: 1, Pyridine–Ac_2O. 2, $LiAlH_4$. 3, 50% AcOH. 4, Dry HCl in C_6H_6. 5, OsO_4. 6, HIO_4. 7, 20% KOH. 8, Conc. HCl in Pr^iOH.

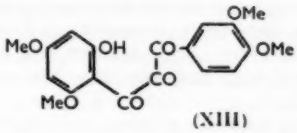
(VIII), as shown by its physical properties, particularly the ultraviolet and infrared spectra. The hydroxylation of the flavene (V) was best effected with osmium tetroxide; an oxidation with monoperphthalic acid gave a mixture of the epoxide, the diol, and (probably) a little of the 3-oxoflavan. Treatment of this mixture with acetic acid followed by acetic anhydride and pyridine gave the crystalline diacetate of compound (VIII), from which the αβ-dihydro-α : 2-dihydroxychalcone (VIII), identical with that obtained after oxidation with osmium tetroxide, was obtained by hydrolysis. Some evidence for the existence of compound (VIII) in the flavan-2 : 3-diol form (IX) was obtained from the results of periodate oxidation. Veratric acid was formed (from the open-chain form, VIII) together with smaller quantities of an ester, presumably (X) (from the cyclic form, IX) which gave more veratric acid after hydrolysis. A further product isolated from the perphthalic oxidation of (VIII) has been formulated tentatively as the dioxo-alcohol (XII). The dihydro-α : 2-dihydroxychalcone (VIII), the corresponding diacetate, and the crude epoxide all gave cyanidin chloride 5 : 7 : 3′ : 4′-tetramethyl ether (XI) on treatment with hydrogen chloride. This anthocyanidin, which has been prepared by Karrer and his co-workers [19] as well as by Hayashi,[20] has been synthesised by condensation of phloroglucinaldehyde dimethyl ether and ω-acetoxyacetoveratrone and the product shown to

[18] Karrer and Fatzer, *Helv. Chim. Acta*, 1942, **25**, 1129.
[19] Karrer, Widmer, Helfenstein, Hürlimann, Nievergelt, and Monserrat-Thoms, *ibid.*, 1927, **10**, 729.
[20] Hayashi, *Acta Phytochim.* (*Japan*), 1934, **8**, 65.

be identical with that derived from dihydro-α : 2-dihydroxy-4 : 6 : 3′ : 4′-tetramethoxychalcone. The flavan-2 : 3-diols or dihydro-α : 2-dihydroxychalcones may thus be regarded as another type of *leuco*anthocyanin, and the original formulation [21] of *leuco*anthocyanins as flavan-2 : 3 : 4-triols is of interest in this connection. The flavan-3 : 4-diols are probably only one of several groups of *leuco*anthocyanins.



(XII)



(XIII)

Aerial oxidation of compound (VIII) gave a product which from analytical evidence appeared to be 1-(3 : 4-dimethoxyphenyl)-3-(2-hydroxy-4 : 6-dimethoxyphenyl)propane-1 : 2 : 3-trione (XIII), a structure which is consistent with the physical evidence. This product failed to yield cyanidin chloride 5 : 7 : 3′ : 4′-tetramethyl ether on treatment with hydrochloric acid in propan-2-ol.

Experimental

Ultraviolet absorption spectra were determined in 95% ethanol except where otherwise stated.

3-(3 : 4-*Dimethoxyphenyl*)*prop*-2-*yn*-1-*ol*.—A suspension of sodium acetylide in liquid ammonia (600 c.c.) was prepared from sodium (13·6 g.) in the usual manner. Redistilled veratraldehyde (83 g.) in purified dioxan (55 c.c.) was added to the sodium acetylide during 1½ hr. while a stream of acetylene was passed through the stirred suspension. The passage of acetylene was continued for another 6 hr., after which ammonium chloride (35 g.) was added and the ammonia allowed to evaporate. The residue was triturated with water and the alcohol (90 g., 94%), m. p. 97—98°, collected by filtration and used in the next stage without further purification. For analysis, the product was sublimed at 90°/0·1 mm. and afforded white needles, m. p. 99·5—100° (lit.,[22] 99°) (Found: C, 68·5; H, 5·95. Calc. for $C_{11}H_{12}O_3$: C, 68·7; H, 6·3%).

3 : 4-*Dimethoxyphenyl Ethynyl Ketone*.—The foregoing alcohol (28·8 g.) in cooled acetone (200 c.c.) was stirred under nitrogen while chromium trioxide (12·45 g.) in water (42 c.c.) and concentrated sulphuric acid (10·5 c.c.) was added at 5° during 1½ hr. After about 1 hr. a crystalline product separated and at this stage acetone (50 c.c.) was added. After the addition of the chromium trioxide, the reaction mixture was stirred for a further 30 min. and then diluted with water (1 l.). The *ketone* which separated was removed by filtration and after crystallisation from aqueous methanol formed colourless needles, m. p. 118·5—119·5° (26·5 g., 93%). For analysis a sample was sublimed at 100°/0·2 mm., forming needles, m. p. 119·5—120° (Found: C, 69·7; H, 5·2. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·3%), $\lambda_{max.}$ 216, 293, and 329 mμ (log ε 4·11, 3·95, and 4·04 respectively), $\lambda_{min.}$ 209, 259, and 306 mμ (log ε 4·10, 3·13, and 3·92 respectively).

Luteolinidin Tetramethyl Ether.—Concentrated sulphuric acid (19 c.c.) was added dropwise to a mixture of phloroglucinol dimethyl ether [23] (11·6 g.) and 3 : 4-dimethoxyphenyl ethynyl ketone (14·3 g.) in glacial acetic acid (190 c.c.). The solution rapidly became dark red and after 4 days a dark red precipitate of the sulphate of luteolinidin tetramethyl ether (28·4 g.) had separated and was removed by filtration. It was converted into the corresponding chloride by 2 crystallisations from 6N-hydrochloric acid. The chloride formed orange needles (24·8 g.), m. p. 161—162° (decomp.; rapid heating) (lit.,[24] m. p. 161—162°) (Found, on a sample dried *in vacuo* at room temperature over solid sodium hydroxide: C, 51·0; H, 6·0; Cl, 9·75; loss in wt. at 120° *in vacuo*, 19·0. Calc. for $C_{19}H_{19}O_5Cl,4·5H_2O,0·25HCl$: C, 50·4; H, 6·3; Cl, 9·8; loss of H_2O and HCl, 19·9%), $\lambda_{max.}$ in ethanol containing 1% of 0·1N-hydrochloric acid: 203, 242, 280, 370, and 492 mμ (log ε 4·54, 4·17, 4·28, 3·70, and 4·62 respectively); $\lambda_{min.}$ 237, 257, 339, and

[21] Robinson and Robinson, *Biochem. J.*, 1933, **27**, 206.
[22] Clapperton and MacGregor, *J. Amer. Chem. Soc.*, 1949, **71**, 3234.
[23] Pratt and Robinson, *J.*, 1924, **125**, 188.
[24] Baker, *J.*, 1929, 1593.

387 mμ (log ε 4·16, 3·94, 3·40, and 3·66 respectively). A further quantity of the product was obtained by dilution of the acetic acid mother-liquors with ether, a gum being precipitated which was treated with boiling ethanol (50 c.c.). The ethanolic solution was decanted from undissolved material, cooled, and saturated with hydrogen chloride. The precipitated solid was separated and crystallised from 6N-hydrochloric acid, giving luteolinidin chloride tetramethyl ether (2 g.), m. p. 161—162° (decomp.).

The ferrichloride formed silky orange-brown needles (from acetic acid), m. p. 206·5—207·5° (lit.,[16] m. p. 206—207°) (Found: C, 43·7; H, 3·9; Fe, 11·4. Calc. for $C_{19}H_{19}O_5Cl_4Fe$: C, 43·5; H, 3·65; Fe, 11·3%), $\lambda_{max.}$ 242, 279, 324, 368, and 492 mμ (log ε 4·32, 4·35, 3·89, 3·96, and 4·58 respectively), $\lambda_{min.}$ 235, 258, 316, 338, and 401 mμ (log ε 4·30, 4·15, 3·88, 3·83, and 3·80 respectively).

2-*Acetoxy*-4 : 6 : 3′ : 4′-*tetramethoxychalcone*.—Luteolinidin tetramethyl ether (1·0 g. of the chloride hydrate) was warmed in pyridine (15 c.c.) for 1 hr. on the water bath. The orange-red solution was cooled, acetic anhydride (15 c.c.) was added, and the mixture kept overnight at room temperature. It was then poured into water (500 c.c.) and after some hours the slightly sticky solid which had separated was collected, washed with water, and dried. Repeated crystallisation from ethanol (charcoal) gave the *chalcone* as pale yellow leaflets (450 mg.), m. p. 154—155°, not depressed on admixture with an authentic specimen prepared by acetylation of 2-hydroxy-4 : 6 : 3′ : 4′-tetramethoxychalcone,[16] m. p. 178—179° (Found: C, 65·0; H, 5·95. $C_{21}H_{22}O_7$ requires C, 65·2; H, 5·75%), $\lambda_{max.}$ 204, 247, and 360 mμ (log ε 4·71, 4·24, and 4·48 respectively), $\lambda_{min.}$ 238 and 271 mμ (log ε 4·11 and 3·60).

5 : 7 : 3′ : 4′-*Tetramethoxyflav*-2-*ene*.—Cooled tetrahydrofuran (300 c.c.) was added to a mixture of luteolinidin chloride tetramethyl ether (13·63 g.; dried at 65° *in vacuo* for 24 hr.) and lithium aluminium hydride (6·62 g.) at −70° and stirring was commenced immediately. The flavylium salt was decolorised rapidly and the temperature of the stirred suspension was slowly raised, until the solvent boiled. The mixture was heated under reflux for 2 hr. After removal of solvent (200 c.c.), the residue was cooled and the excess of lithium aluminium hydride destroyed by the addition of wet ether (300 c.c.). The product was then shaken with 25% aqueous sodium potassium tartrate (200 c.c.), and the aqueous layer removed and repeatedly extracted with 50 c.c. portions of ether. The combined ethereal fractions were washed with aqueous sodium potassium tartrate (3 × 50 c.c.) and then dried and the solvent removed to give a pink residue (10·6 g.). Crystallisation from ether gave pink needles (8·23 g.), m. p. 114—116° raised to 118·5—119° after two further crystallisations from ethanol. Careful purification of material obtained from mother-liquors gave the product as pinkish blades (total yield, 9·03 g., 73%). Sublimation at 105—107°/0·05 mm. gave colourless prisms, m. p. 119·5° (lit.,[12] m. p. 119°), which were crystallised from ethanol before analysis (Found: C, 69·4; H, 6·3. Calc. for $C_{19}H_{20}O_5$: C, 69·5; H, 6·15%), $\lambda_{max.}$ 209, 247, 273, and 292 mμ (log ε 4·73, 4·29, 3·90, and 3·82 respectively), $\lambda_{min.}$ 241 and 290 mμ (log ε 4·28 and 3·81).

αβ-*Dihydro*-2-*hydroxy*-4 : 6 : 3′ : 4′-*tetramethoxychalcone*.—A solution of 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene (300 mg.) in aqueous acetic acid (15 c.c. of 50%) was heated on the water bath for 2 hr., then cooled, and the crystalline product (285 mg.) separated and crystallised from ethanol to give the dihydrochalcone as colourless needles, m. p. 137·5—138° (lit., 137°) undepressed on admixture with a sample prepared as described by Freudenberg *et al.*[25] (Found: C, 66·0; H, 6·4. Calc. for $C_{19}H_{22}O_6$: C, 65·9; H, 6·4%), $\lambda_{max.}$ 206, 227, 273, and 303 mμ (log ε 4·81, 4·54, 4·08, and 3·94 respectively), $\lambda_{min.}$ at 221, 246, and 292 mμ (log ε 4·43, 3·54, and 3·90 respectively). The infrared spectrum of a solution in chloroform showed bands in the carbonyl region at 1592, 1621, 1659, and 1716 (w) cm.$^{-1}$. The methyl ether, 2 : 4 : 6 : 3′ : 4′-pentamethoxydihydrochalcone (obtained by use of methyl sulphate and potassium carbonate in acetone), formed colourless needles, m. p. 113·5—114° (lit.,[25] 113—114°), from methanol (Found: C, 66·9; H, 6·8. Calc. for $C_{20}H_{24}O_6$: C, 66·7; H, 6·7%), $\lambda_{max.}$ 207, 228, 273, and 303 mμ (log ε 4·72, 4·40, 4·10, and 3·93 respectively), $\lambda_{min.}$ 219, 248, and 292 mμ (log ε 4·30, 3·60, and 3·89 respectively). The *acetyl derivative* (prepared by acetic anhydride–pyridine) formed white felted needles, m. p. 126·5—127° (from methanol) (Found: C, 65·3; H, 6·2; Ac, 11·8. $C_{19}H_{21}O_6{\cdot}CO{\cdot}CH_3$ requires C, 64·9; H, 6·2; Ac, 11·1%), $\lambda_{max.}$ 204, 228, 274, and 303 mμ (log ε 4·65, 4·38, 4·08, and 3·88 respectively), $\lambda_{min.}$ 217, 246, 293 mμ (log ε 4·26, 3·40, and 3·85 respectively). The infrared spectrum of a chloroform solution showed bands at 1595, 1620, 1671, and 1762 cm.$^{-1}$.

[25] Freudenberg, Fikentscher, and Wenner, *Annalen*, 1925, **442**, 309.

Formation of Flavylium Salts from 5 : 7 : 3′ : 4′-Tetramethoxyflav-2-ene.—(*a*) A solution of ferric chloride (500 mg.) in concentrated hydrochloric acid (1·5 c.c.) was added to a solution of the flavene (110 mg.) in glacial acetic acid (5 c.c.). After 2 days at room temperature, the crystalline precipitate was collected and crystallised from acetic acid to yield luteolinidin tetramethyl ether ferrichloride (72·4 mg., 41%), m. p. alone and mixed with the sample described above, 206·5—207·5°. (*b*) A solution of the flavene (100 mg.) in benzene (2 c.c.) was saturated with dry hydrogen chloride and kept at room temperature for 3 days. The orange-red precipitate was collected and crystallised from 6N-hydrochloric acid to yield luteolinidin tetramethyl ether chloride (40 mg.), m. p. and mixed m. p. 161—162°.

Apigeninidin Chloride Trimethyl Ether; 5 : 7 : 4′-Trimethoxyflavylium Chloride.—Ethynyl *p*-methoxyphenyl ketone, m. p. 87—88° (Found: C, 74·9; H, 4·9. Calc. for $C_{19}H_{8}O_{2}$: C, 74·9; H, 5·1%), $\lambda_{max.}$ 223 and 305 mμ (log ε 4·00 and 4·23), was prepared by the method of Irving and Johnson [25] by oxidation of 3-*p*-methoxyphenylprop-2-ynol, m. p. 36—37°. Concentrated sulphuric acid (18 c.c.) was added dropwise to a solution of phloroglucinol dimethyl ether (12·4 g.) and ethynyl *p*-methoxyphenyl ketone (11·5 g.) in cooled (10°) glacial acetic acid (180 c.c.). The solution rapidly became dark red, and after 5 days the dark red precipitate of apigeninidin sulphate trimethyl ether (34·2 g.) was collected, washed with ether, and twice crystallised from 6N-hydrochloric acid to yield the corresponding chloride (22·8 g.) as orange needles, m. p. 135—136°, of a *hydrate* which still contained hydrogen chloride (Found: C, 55·6; H, 5·95; Cl, 11·4; loss at 100° *in vacuo*, 15·0. $C_{18}H_{17}O_{4}Cl,2{\cdot}5H_{2}O,0{\cdot}25HCl$ requires C, 55·9; H, 5·8; Cl, 11·5; loss of H_2O and HCl, 15·5%). King *et al.*[13] record m. p. 159—160° (decomp.), for a pentahydrate. Light absorption in ethanol containing 1% of N-hydrochloric acid: max. at 205, 242, 277, 325, and 474 mμ (log ε 4·55, 3·96, 4·29, 3·72, and 4·59 respectively); min. at 236, 249, 303, and 346 mμ (log ε 3·94, 3·92, 3·54, and 3·12 respectively). The ferrichloride separated from acetic acid as red-brown prisms, m. p. 185—186° (with sintering at 181°) (lit.,[16] 187° with sintering at 180°) (Found: C, 43·5; H, 3·6; Fe, 10·6. Calc. for $C_{18}H_{17}O_{4}Cl_{4}Fe$: C, 43·7; H, 3·5; Fe, 10·6%), $\lambda_{max.}$ 204, 242, 277, 326, and 475 mμ (log ε 4·59, 4·23, 4·38, 3·99, and 4·54 respectively), $\lambda_{min.}$ 234, 251, 305, and 345 mμ (log ε 4·21, 4·18, 3·88, and 3·80).

5 : 7 : 4′-Trimethoxyflav-2-ene.—Apigeninidin trimethyl ether (hydrated salt dried at 65° *in vacuo* for 24 hr.; 4·05 g.) in tetrahydrofuran (120 c.c.) was treated with lithium aluminium hydride (2·02 g.) and the mixture worked up essentially as described above for the preparation of 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene. Removal of solvent at 15° under reduced pressure in a stream of nitrogen afforded a pink solid which was treated with boiling light petroleum in a nitrogen atmosphere, the suspension cooled at 0° for 4 hr., and the insoluble material (50 mg.) separated. The solvent was removed from the filtrate to give a pink residue (3·02 g.) which separated from ethanol as an amorphous solid, m. p. 119—123°. Repeated purification of this material from ethanol followed by sublimation (120°/1 mm. for 4 days) gave colourless prisms, m. p. 130·5—131° (sintering at 128°) (lit.,[13] 129—130°) which was not raised after further crystallisation from ethanol (Found: C, 72·5; H, 6·1. Calc. for $C_{18}H_{18}O_{4}$: C, 72·5; H, 6·1%). A mixture of this product with a sample kindly supplied by Dr. J. W. Clark-Lewis had m. p. 128—130°. Light absorption max. were at 204, 222, 247, and 272 mμ (log ε 4·68, 4·41, 4·40, and 3·90 respectively) and min. at 218, 235, and 266 mμ (log ε 4·41, 4·33, and 3·89). The infrared spectrum of a solution in carbon tetrachloride showed max. at 3066, 2997, 2951, 2911, 2865, 2842, 1467, 1458, 1440, 1419, 1346, 1331, and 1305 cm.$^{-1}$. Another determination (KBr disc) gave a spectrum which was identical with that of the authentic specimen.

5 : 7 : 3′ : 4′-Tetramethoxyflavan-2 : 3-diol; αβ-Dihydro-α : 2-dihydroxy-4 : 6 : 3′ : 4′-tetramethoxychalcone.—(*a*) A solution of 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene (540 mg.) in dry benzene (12 c.c.) was added to a solution of osmium tetroxide (420 mg.) in a mixture of benzene (6 c.c.) and pyridine (0·6 c.c.). The solution darkened and a slight precipitate was observed after 2 hr. The mixture was kept in the dark until deposition of solid had ceased (5 days), then it was diluted with ether (25 c.c.) and kept overnight and the light brown crystalline complex separated and washed with ether. This complex was dissolved in warm methylene dichloride (25 c.c.), and the solution cooled and shaken with 2% aqueous potassium carbonate solution (100 c.c.) containing mannitol (10 g.) until the colour of the organic phase ceased to fade (48 hr.). The aqueous phase was then replaced by fresh potassium carbonate–mannitol reagent, and agitation continued until the organic phase was colourless (24 hr.). Ether (150 c.c.) was added and the aqueous layer removed. This was extracted with ether (2 × 25 c.c.), and the combined

[25] Irving and Johnson, *J.*, 1948, 2037.

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organic layers were washed and dried. Removal of the solvent at <28° under reduced pressure in an atmosphere of nitrogen left a residue which was treated with ether and most of the ether removed to give αβ-*dihydro*-α : 2-*dihydroxy*-4 : 6 : 3′ : 4′-*tetramethoxychalcone* (474 mg., 78%) as pale yellow crystals, m. p. 111—113°. The ethereal mother-liquors were clarified with charcoal and cautiously diluted with light petroleum (b. p. 60—80°) to give a further quantity of the product (60 mg.) as colourless needles, m. p. 111—113°. It recrystallised from benzene–light petroleum as colourless leaflets, m. p. 88—90° (with previous darkening), which contained solvent of crystallisation (Found: C, 65·7; H, 6·15. $C_{19}H_{22}O_7,\frac{1}{2}C_6H_6$ requires C, 65·8; H, 6·3%). Slow crystallisation from ethyl acetate–light petroleum, chloroform–light petroleum, or ether–light petroleum afforded white felted needles, m. p. 113—114° (sintering >110°), which after further crystallisation from cold aqueous methanol gave the product as colourless silky needles, m. p. 114·5—115° (Found: C, 62·9; H, 6·15. $C_{19}H_{22}O_7$ requires C, 63·0; H, 6·12%), $\lambda_{max.}$ 207, 229, 276, and 307 mμ (log ε 4·73, 4·37, 4·00, and 3·88 respectively), $\lambda_{min.}$ 220, 249, and 294 mμ (log ε 4·30, 3·59, and 3·83 respectively). The infrared spectrum of a solution in chloroform showed main max. at 3324, 3070, 2986, 2941, 2839, 1673, 1628, and 1601 cm.$^{-1}$, and of the solid (KBr disc) at3503, 3413, 3293, 3092, 2930, 2832, 1653,1624, 1590, and 1518 cm.$^{-1}$. The product was readily soluble in the common organic solvents, except light petroleum in which it was sparingly soluble. It dissolved completely in dilute aqueous sodium hydroxide to give a colourless solution which soon became yellow and after warming changed to a pale orange colour. Heating an ethanolic solution with concentrated hydrochloric acid gave a bright cherry-red colour which is attributed to anthocyanidin formation. A bright red colour was also obtained with the vanillin reagent.[27]

(*b*) αβ-Dihydro-α : 2-diacetoxy-4 : 6 : 3′ : 4′-tetramethoxychalcone monohydrate (264 mg.; see below), anhydrous potassium acetate (3·0 g.), and oxygen-free absolute methanol (30 c.c.) were heated under reflux in an atmosphere of nitrogen for 14 hr. The yellow solution was evaporated under reduced pressure at 25—28° and the residue shaken with water (30 c.c.) and ether (100 c.c.). The aqueous layer was separated, washed with ether (2 × 10 c.c.), and then rejected; the combined ethereal extracts were washed and dried and the solvent was removed under reduced pressure as in the previous experiment. The residual bright yellow solid was treated with a small amount of methanol and filtered from a small quantity of a yellow oxidation product (0·8 mg.; see below), and the filtrate diluted with ether and evaporated as above. Crystallisation of the residue thrice from benzene–light petroleum (charcoal) and once from chloroform–light petroleum yielded αβ-dihydro-α : 2-dihydroxy-4 : 6 : 3′ : 4′-tetramethoxychalcone as white felted needles (39 mg., 18%), m. p. 113—114° alone and when mixed with the product from the previous experiment.

(*c*) A portion of the solid (100 mg.) obtained from the action of monoperphthalic acid on 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene (see below) was dissolved in benzene (2 c.c.), the solution clarified with charcoal, and the hot solution diluted with light petroleum (2 c.c.). The colourless solution was decanted from the precipitated gum and slowly diluted with an equal volume of light petroleum. The solid so obtained was collected and after crystallisation from ether–light petroleum gave αβ-dihydro-α : 2-dihydroxy-4 : 6 : 3′ : 4′-tetramethoxychalcone as colourless needles, m. p. 113—114°, identical with the products of the two previous experiments.

α : 2-*Diacetoxy*-αβ-*dihydro*-4 : 6 : 3′ : 4′-*tetramethoxychalcone*.—(*a*) The product of the foregoing experiment was acetylated with acetic anhydride and pyridine at room temperature to yield the *diacetyl derivative* as colourless needles, m. p. 148·5—149°, of the monohydrate (Found: C, 59·5; H, 5·95; loss on drying at 65° *in vacuo*, 3·4. $C_{23}H_{26}O_9,H_2O$ requires C, 59·5; H, 6·05; H_2O, 4·5. Found, on a sample dried at 65° *in vacuo*: C, 61·6; H, 5·7. $C_{23}H_{26}O_9$ requires C, 61·9; H, 5·8%), $\lambda_{max.}$ 204, 229, 278, and 307 mμ (log ε 4·73, 4·41, 4·13, and 3·95 respectively), $\lambda_{min.}$ 218, 249, and 296 mμ (log ε 4·30, 3·54, and 3·92 respectively). The infrared spectrum of a chloroform solution showed bands in the carbonyl region at 1600, 1622, 1686, 1742, and 1765 cm.$^{-1}$.

(*b*) An ethereal solution of monoperphthalic acid (832 mg.; 3 mol.) was added to 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene (500 mg.) in ether (150 c.c.), and the solution diluted with dry ether (to 250 c.c.) and kept at 18° with occasional shaking for 80 min. Acidic material was removed by shaking the mixture with the calculated quantity of aqueous sodium hydrogen carbonate, and the resulting ethereal layer was separated and dried. The solvent was removed at room temperature under reduced pressure in an atmosphere of nitrogen. The residue (480 mg.),

[27] Bate-Smith and Swain, *Chem. and Ind.*, 1953, 377.

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which rapidly assumed a bright orange-red colour when exposed to air, was dissolved in acetic acid (5 c.c.) containing anhydrous potassium acetate (300 mg.) and acetic anhydride (1 c.c.). This solution was kept at room temperature overnight, then cooled (ice), and pyridine (10 c.c.) and acetic anhydride (4 c.c.) were added. After a further 24 hr. at room temperature, the solution was poured into cold water and the precipitated solid collected. After two crystallisations from methanol, α : 2-diacetoxy-αβ-dihydro-4 : 6 : 3′ : 4′-tetramethoxychalcone (469 mg., 69%) formed colourless needles, m. p. 148·5—149°, identical with the product of the previous experiment. It gave a bright cherry-red colour with the vanillin reagent [27] or when warmed with concentrated hydrochloric acid.

Periodate Oxidation of αβ-Dihydro-α : 2-dihydroxy-5 : 7 : 3′ : 4′-tetramethoxychalcone.—5% Aqueous sodium metaperiodate (3·28 c.c.) was added in small quantities during 36 hr. to αβ-dihydro-α : 2-dihydroxy-5 : 7 : 3′ : 4′-tetramethoxychalcone (VIII) (300 mg.) dissolved in methanol (7 c.c.), and the mixture kept overnight at room temperature. The product was diluted with water (10 c.c.) and exhaustively extracted with ether. The ethereal extract was shaken with sodium hydrogen carbonate solution and from the ethereal layer phenolic and neutral fractions were isolated in the usual manner. The crystalline solid obtained by acidification of the sodium hydrogen carbonate layer was collected and crystallised from water, to give veratric acid (73 mg.) as colourless needles, m. p. and mixed m. p. 179—180°. A further quantity of veratric acid (15 mg.) was obtained by ether-extraction of the mother-liquors and vacuum-sublimation of the product.

The neutral fraction from the oxidation was obtained as a partially crystalline colourless gum (79 mg.) which was hydrolysed by warm 20% aqueous potassium hydroxide (5 c.c.) in an atmosphere of nitrogen until dissolution was complete. The orange-red solution was cooled and the acidic material isolated in the usual manner. The crude veratric acid thus obtained was purified as above and afforded the pure acid (35 mg.) as colourless prisms, m. p. 179—180°. The overall yield of veratric acid was thus 123 mg. (81%).

Cyanidin Chloride 5 : 7 : 3′ : 4′-Tetramethyl Ether.—(*a*) αβ-Dihydro-α : 2-dihydroxy-5 : 7 : 3′ : 4′-tetramethoxychalcone (25 mg.) was heated in propan-2-ol–concentrated hydrochloric acid (19 : 1; 25 c.c.) in a sealed tube for 1½ hr. The product was cooled, diluted with ether (75 c.c.), and then brought on to a cellulose (Solka-Floc) column (170 × 20 mm.). Preliminary elutions were carried out with propan-2-ol–ether (1 : 4; 250 c.c.) containing concentrated hydrochloric acid (5 c.c.) and then ether (100 c.c.) containing saturated methanolic hydrogen chloride (3 c.c.). The main product was eluted from the column with the upper phase of butan-1-ol–2N-hydrochloric acid (1 : 1) and after an initial pale purple eluate of phlobaphene had been obtained and rejected the main fraction of anthocyanidin plus phlobaphene (*ca.* 20 c.c.) was collected and combined with that obtained from a second similar experiment starting from 25 mg. of the dihydrochalcone. The solvent was removed from the combined eluates under reduced pressure at 18° as rapidly as possible, care being taken to ensure that an excess of hydrogen chloride was always present by the frequent additions of small amounts of saturated methanolic hydrogen chloride. The residue was again chromatographed on a cellulose column (180 × 20 mm.), the butanol–hydrochloric acid upper phase being used for elution as before. After separation of the purple phlobaphene band, the anthocyanidin was eluted as a broad red band. It was diluted (to 50 c.c.) with concentrated hydrochloric acid (2·5 c.c.) and the hydrochloric acid–butanol upper layer, and a determination of the light absorption of the resulting solution and comparison with a standard solution indicated that the anthocyanidin content was 2·44 mg. Removal of the solvent gave a red residue which showed R_F values identical with those of authentic cyanidin chloride 5 : 7 : 3′ : 4′-tetramethyl ether when subjected to chromatography on paper. A further quantity of the product was isolated from the propanol–ether eluates of the two reaction products, and the total yield of the anthocyanidin was 4·1 mg. (6·8%). The acid solutions of the anthocyanidin faded rapidly and as a result a spectrophotometric determination gives a minimum figure.

Similar reactions were carried out on α : 2-diacetoxy-αβ-dihydro-4 : 6 : 3′ : 4′-tetramethoxychalcone, and the crude product from the action of monoperphthalic acid on 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene (above). The products were shown to be identical with cyanidin 5 : 7 : 3′ : 4′-tetramethyl ether by chromatography on paper. Streaks at the solvent fronts caused by the presence of traces of phlobaphene were observed. Formation of the anthocyanidin was slightly faster from the diol than from its diacetate, and considerably faster from the crude oxide than from the diol.

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(*b*) A cooled (0°) solution of 2-hydroxy-4 : 6-dimethoxybenzaldehyde (1·01 g.) and ω-acetoxy-3 : 4-dimethoxyacetophenone (below) (1·15 g.) in dry ethyl acetate (12·5 c.c.) and dry ethanol (3 c.c.) was saturated with hydrogen chloride during 3 hr. and the dark red solution stored in the dark at room temperature for 7 days. Ether (17 c.c.) was then added cautiously and the mixture kept in the refrigerator for 14 days. The trihydrate of cyanidin chloride 5 : 7 : 3′ : 4′-tetramethyl ether was obtained as black prisms with a green reflex, m. p. 192—196° with previous sintering (Found: C, 54·5; H, 6·0; Cl, 8·8; loss at 100° *in vacuo*, 11·8. Calc. for $C_{19}H_{19}O_6Cl,3H_2O$: C, 54·7; H, 6·0; Cl, 8·5; H_2O, 13·0%). After crystallisation from ethanol–concentrated hydrochloric acid (1 : 1) the trihydrate was obtained as small felted carmine needles, m. p. 201—202° with previous sintering (Found: C, 54·8; H, 5·7; Cl, 8·4; loss at 100° *in vacuo*, 13·8%). Hayashi [20] records decomp. 200° for a dihydrate. Light absorption: (i) in ethanol containing 1% of N-hydrochloric acid, max. at 270, 335, 385, and 535 mμ (log ε 4·38, 3·55, 3·63, and 4·60 respectively) with a shoulder at 320—355 mu [log ε (mean) 3·57], min. at 250, 352, and 400 mμ (log ε 4·26, 3·33, and 3·61 respectively); (ii) in the butan-1-ol–2N-hydrochloric acid (1 : 1) upper layer containing 5% of concentrated hydrochloric acid, max. at 276, 385, and 532 mμ (log ε 4·28, 3·59, and 4·54 respectively), min. at 345 and 397 mμ (log ε 3·44 and 3·60). After this solution had been kept in the dark for 3 days the intensity (log ε) of the max. at 532 mμ had dropped to 4·42. The perchlorate formed fine purple-red needles, m. p. 255—256° (decomp.) (from glacial acetic acid) (Found: C, 51·5; H, 4·3. $C_{19}H_{19}O_{10}Cl$ requires C, 51·5; H, 4·4%).

Phloroglucinaldehyde 2 : 4-*Dimethyl Ether*.—A stirred and cooled (−10°) mixture of phloroglucinol dimethyl ether (10·2 g.) and zinc cyanide [28] (12 g.) in anhydrous ether (250 c.c.) was saturated with dry hydrogen chloride during 3 hr. and then allowed to warm to room temperature. Next day the sticky imine hydrochloride was collected, washed with ether, and triturated with water (50 c.c.). The resulting amorphous precipitate was separated, washed with a little water, then ether, and dissolved in boiling 50% v/v aqueous methanol (450 c.c.). After filtration, the solution was heated to *ca.* 65° for ½ hr., then cooled, and the crystalline precipitate which separated was collected and twice recrystallised from aqueous methanol to yield the product (8·24 g.) as colourless needles, m. p. 71°. The combined aqueous methanol mother-liquors were reduced to *ca.* 300 c.c. under reduced pressure, then cooled, and the precipitated solid was collected. This was treated with a small quantity of ether, the insoluble material was separated, and after removal of the solvent the residue was distilled in steam. The colourless needles which were obtained in the distillate were separated and crystallised from aqueous methanol to give a further quantity (1·92 g.) of the aldehyde (total yield, 10·16 g., 83%; lit.,[13] 30%) (Found: C, 59·3; H, 5·75. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%).

ω-*Diazo*-3 : 4-*dimethoxyacetophenone*.—Freshly prepared veratroyl chloride (13·5 g.) in dry chloroform (25 c.c.) was added dropwise during 1 hr. to a cooled (5°) solution of diazomethane (from 42 g. of *N*-nitrosomethylurea) in ether (300 c.c.). When evolution of nitrogen had ceased, the yellow silky needles (10·1 g.), m. p. 76—77° (decomp.), were collected, and light petroleum (500 c.c.) was added to the filtrate which was then evaporated at room temperature to small volume in a stream of air. The yellow solid which separated was collected and crystallised twice from light petroleum to give a further quantity (2·5 g.), m. p. 77—78° (decomp.), of ω-*diazo*-3 : 4-*dimethoxyacetophenone* (total yield, 12·6 g., 91%). For analysis, a small quantity was recrystallised from light petroleum to give the product as pale yellow silky needles, m. p. 77·5—78° (Found: C, 58·2; H, 4·8; N, 13·0. $C_{10}H_{10}O_3N_2$ requires C, 58·2; H, 4·9; N, 13·6%).

ω-*Acetoxy*-3 : 4-*dimethoxyacetophenone*.—The foregoing diazo-ketone (5·05 g.) and glacial acetic acid (35 c.c., containing 0·5 g. of fused potassium acetate) were heated, with frequent shaking, at 70° until evolution of nitrogen ceased. The golden-brown solution was poured into water (150 c.c.), and the clear solution was extracted with ether. The ethereal extract was shaken with aqueous sodium hydrogen carbonate solution, dried, and evaporated. The residual gum was triturated with methanol in order to induce crystallisation. The solid product was collected, and crystallised from methanol, then ether, to yield colourless rhombs of ω-acetoxy-3 : 4-dimethoxyacetophenone (4·82 g., 83%), m. p. 85·5—86·5°, raised to 86—87° by further crystallisation from ether or methanol (values between 82·5—83·5 and 91—92° have been recorded for the m. p.) (Found: C, 60·3; H, 5·9. Calc. for $C_{12}H_{14}O_5$: C, 60·5; H, 5·9%).

[28] Adams and Levine, *J. Amer. Chem. Soc.*, 1923, **45**, 2373.

1-(3 : 4-*Dimethoxyphenyl*)-3-(2-*hydroxy*-4 : 6-*dimethoxyphenyl*)*propane*-1 : 2 : 3-*trione*.—5 : 7 : 3′ : 4′-Tetramethoxyflav-2-ene (570 mg.) was treated with osmium tetroxide (398 mg.) as described above. The resulting complex was decomposed in the same manner as previously and the colourless ether–methylene dichloride solution of the dihydrodihydroxychalcone separated and kept in the dark for 24 days, during which it became yellow. The solvent was removed at <25° under reduced pressure in a stream of nitrogen and the pale yellow residue triturated with methanol (3 c.c.). The undissolved solid was separated, washed with methanol, and crystallised from ethanol to give the presumed *trione* (8 mg.) as bright yellow leaflets, m. p. 197·5—199° (Found, on a sample dried at 130° *in vacuo*: C, 61·5; H, 5·0. $C_{19}H_{18}O_8$ requires C, 61·0; H, 4·85%), $\lambda_{max.}$ (in dioxan) 231 and 281 mμ (log ε 4·19 and 4·30), $\lambda_{min.}$ 247 mμ (log ε 3·52). Intense bands in the infrared spectrum (KBr) in the carbonyl region were observed at 1592, 1606, 1634, 1645, 1663, and 1687 cm.$^{-1}$. An ethanolic solution of the oxidation product gave an orange-brown colour when heated with concentrated hydrochloric acid and the resulting solution was shown not to contain cyanidin chloride tetramethyl ether by paper chromatographic examination. Small yields of the same oxidation product have been isolated from an oxidation of the flavene (V) with monoperphthalic acid, from an aerial oxidation of an ethereal solution of the αβ-dihydro-α : 2-dihydroxychalcone (VIII), and from the deacetylation of α : 2-diacetoxy-αβ-dihydro-4 : 6 : 3′ : 4′-tetramethoxychalcone with potassium acetate (see above).

3-*Hydroxy*-1-(3 : 4-*dimethoxyphenyl*)-3-(2-*hydroxy*-4 : 6-*dimethoxyphenyl*)*propane*-1 : 2-*dione*.—An ethereal solution of monoperphthalic acid (1·36 g., 5 mol.) was added to 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene (500 mg.; 1 mol.) in anhydrous ether, and the mixture diluted with ether (to 250 c.c.) and cooled in the refrigerator. After 7 and 14 days, further quantities of monoperphthalic acid (278 mg., 1 mol.) were added, and after 3 weeks the ethereal solution was decanted from the solid which was dissolved in chloroform (10 c.c.), and the combined solutions were washed with aqueous sodium hydrogen carbonate and dried. The solvent was removed at <25° at reduced pressure in an atmosphere of nitrogen to leave a sticky product which was triturated with methanol and washed with methanol to remove all soluble products. The yellow residue (116 mg.) was fractionally crystallised from small quantities of ethanol–chloroform to yield sparingly soluble bright yellow leaflets and moderately soluble pale yellow needles. The former product was identical with that described in the foregoing experiment. The mother-liquors from the crystallisation, after evaporation to small bulk, yielded a further quantity of the second product which was mixed with the main crop and crystallised from ethanol to give the *hydroxy-diketone* (51·6 mg.) as pale yellow needles, m. p. 174—175° (Found: C, 61·0; H, 5·65. $C_{19}H_{20}O_8$ requires C, 60·65; H, 5·35%). The intensities of the light absorption bands varied rapidly on keeping but the following are the highest values observed: max. at 203—206, 228, and 282—284 mμ (log ε 4·60, 4·40, and 4·37 respectively) with min. at 219—220 and 250 mμ (log ε 4·31 and 3·84). Prominent bands in the infrared spectrum ($CHCl_3$ solution) were obtained at 1606, 1649, and 1685 cm.$^{-1}$. An ethanol solution of the compound gave a cerise colour when treated with magnesium and concentrated hydrochloric acid but not with the acid alone. A low yield of the same compound has also been isolated after reaction of perbenzoic acid with 5 : 7 : 3′ : 4′-tetramethoxyflav-2-ene.

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Department of Chemistry, The University, Nottingham. [*Received, May 27th*, 1958.]

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814. *The Oxidation of Proline, Hydroxyproline, and* N-*Methylglycine with Periodate.*

By P. D. Bragg and L. Hough.

Proline, hydroxyproline, and *N*-methylglycine react with periodate and undergo oxidative decarboxylation, proline giving Δ^1-pyrroline which is further oxidised to pyrrolid-2-one.

Structural investigations of the carbohydrate components of ovomucoid and ovalbumin have revealed that the mucoproteins react with more sodium metaperiodate than can be accounted for by the carbohydrate alone.[1] Similar results were obtained with starch–protein mixtures containing more than 23% of protein.[2] The protein of the jelly-coat substance of *Echinocardium cylindrica* is oxidised by periodate at the cysteine, cystine, tryptophan, and tyrosine residues.[3] Ovalbumin was oxidised with similar results.[4] The reactions of various amino-acids with periodate have been examined and at room temperature serine, threonine, methionine, and cystine were rapidly oxidised.[5] At 100°, other amino-acids reacted with the formation of aldehydes by processes involving oxidative decarboxylation and deamination, but secondary reactions were also significant.[6] Examination of mucoprotein hydrolysates on paper chromatograms using a periodate–*p*-anidisine method for the detection of the carbohydrates, revealed that hydroxyproline was rapidly oxidised by periodate. The periodate–*p*-anisidine method of detection was devised as an alternative to the periodate–benzidine [7] and periodate–starch iodide [8] spray reagents.

The reaction of hydroxyproline with periodate prompted a quantitative study of this and other amino-acids with sodium metaperiodate at room temperature and in the dark. Glycine, alanine, phenylalanine, *N*-acetylglycine, and glycylglycine showed no significant reaction: histidine, proline, and hydroxyproline were rapidly oxidised and *N*-methylglycine (sarcosine) also consumed periodate at a slow but significant rate. The p*K* values for proline, hydroxyproline, and *N*-methylglycine (10·01, 10·60, and 9·73 respectively) reveal that they are more basic than the other common amino-acids,[9] suggesting that the imino-groups are involved in the reaction and that the rate of oxidation of the amino-acid depends upon the basicity of this group.

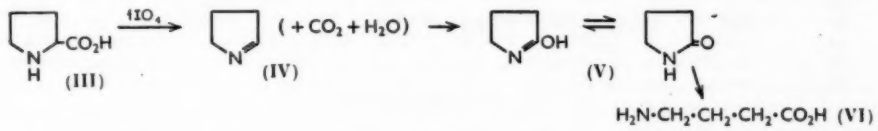
N-Methylglycine (I) reacted with 1 mol. of periodate in *ca.* 70 hr. with the formation of carbon dioxide and formaldehyde, in agreement with oxidation to the *N*-methylene derivative (II) and carbon dioxide, followed by hydrolysis to formaldehyde and methylamine.

$$\underset{\text{(I)}}{Me{\cdot}NH{\cdot}CH_2{\cdot}CO_2H} \xrightarrow{IO_4} \underset{\text{(II)}}{Me{\cdot}N{:}CH_2} (+ CO_2 + H_2O) \longrightarrow Me{\cdot}NH_2 + CH_2O$$

The reaction of proline (III) with periodate (2 mol.) occurred in two stages. The first mol. was consumed rapidly (3 hr.) with concomitant release of 1 mol. of carbon dioxide, whereas the second mol. of oxidant reacted slowly (24 hr.); no acid was liberated. The second stage was pH-dependent since at pH 2·2 only 1 mol. of oxidant was consumed, whereas 2 mol. were consumed at pH 10·2. Ether-extraction of an equimolar mixture of proline and periodate afforded Δ^1-pyrroline (IV). This product was characterised by the formation of a complex with mercuric chloride in dilute aqueous solution [10] and by catalytic

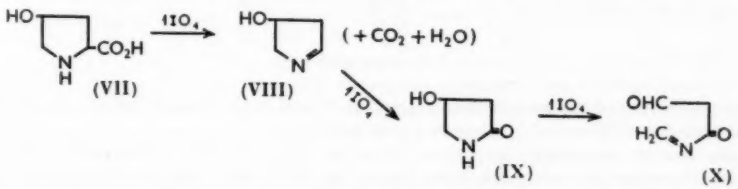
[1] Bragg and Hough, unpublished results.
[2] Anderson, Greenwood, and Hirst, *J.*, 1955, 225.
[3] Vasseur, *Acta Chem. Scand.*, 1952, **6**, 376.
[4] Maekawa and Kushibe, *Bull. Chem. Soc. Japan*, 1954, **27**, 277; *Chem. Abs.*, 1955, **49**, 9698.
[5] Nicholet and Shinn, *J. Amer. Chem. Soc.*, 1939, **61**, 1615; *J. Biol. Chem.*, 1941, **139**, 687.
[6] Fleury, Courtois, and Grandchamp, *Bull. Soc. chim. France*, 1949, **16**, 88.
[7] Cifonelli and Smith, *Analyt. Chem.*, 1954, **26**, 1132.
[8] Metzenberg and Mitchell, *J. Amer. Chem. Soc.*, 1954, **76**, 4187.
[9] "Amino Acids and Proteins," ed. D. M. Greenberg, Charles C. Thomas, Springfield, Illinois, U.S.A., 1951, p. 430.
[10] Langheld, *Ber.*, 1909, **42**, 2360; Krimm, Ph.D. Thesis, Darmstadt, 1950.

hydrogenation to pyrrolidine which was identified as the characteristic *N*-toluene-*p*-sulphonyl derivative.[11] The pyrroline readily polymerised, a property typical[10] of Δ^1-pyrroline (IV). Contrary to previous belief, Murray and Cloke[12] have shown that Δ^1- and Δ^2-pyrrolines are not in tautomeric equilibrium. Since glycylproline was not oxidised by periodate it follows that the imino-nitrogen atom of proline must be unsubstituted for oxidation to occur. Thus the first stage in the reaction of periodate with proline involves oxidative decarboxylation to Δ^1-pyrroline (IV). The subsequent product from the oxidation of Δ^1-pyrroline (IV) was identified as pyrrolid-2-one (V) by isolation in good yield as the hydrochloride and by acid-hydrolysis to γ-aminobutyric acid[13] (VI). At pH 10·2 pyrrolid-2-one (V) appeared to be the sole product after the consumption of 2 mol. of periodate, whereas at pH 2·2 only a trace (<1%) was found. Pyrrolid-2-one



and pyrrolidine were not oxidised by periodate. The conversion of Δ^1-pyrroline (IV) into pyrrolid-2-one (V) represents a novel type of periodate oxidation and, since the reaction was impeded in acid, quaternary ammonium salt formation was probably responsible.

In unbuffered solution hydroxyproline (VII) was extensively oxidised by 4 mol. of periodate (24 hr.) in agreement with the results of Carter and Loo,[14] with the formation of 1·33 equivalents of acid, 0·44 mol. of ammonia, 0·83 mol. of formaldehyde and 1·9 mol. of carbon dioxide. The first mol. of carbon dioxide appeared early in the reaction (2 hr.), suggesting that the first step, as with proline, was oxidative decarboxylation to hydroxypyrroline (VIII). At pH 2, only 3 mol. of periodate reacted with the liberation of 0·95 mol. of carbon dioxide, but no formaldehyde was detected. An acid-stable *N*-methylene derivative may have been formed by oxidative cleavage of 4-hydroxypyrrolid-2-one (IX).



Various routes could be suggested for the oxidation of hydroxyproline, but further evidence is required to elucidate the pathway subsequent to oxidative decarboxylation. The periodate reaction differs, however, from the action on hydroxyproline of either hydrogen peroxide in the presence of alkaline copper sulphate or catalase and amino-acid oxidase, both of which led to the formation of pyrrole-2-carboxylic acid.[15] This acid did not react with periodate and was not detected in the periodate oxidation mixtures by the sensitive paper-chromatographic technique.

Experimental

Quantitative Measurements.—The amino-acid (*ca.* 20 mg.; accurately weighed) was dissolved in water (50 ml.), then dilute sulphuric acid (50 ml.) or borate buffer (50 ml.; pH 10·2) and 0·3M-sodium metaperiodate solution (3 ml.) were added. Aliquot portions (5 ml.) were removed

[11] Mann and Smithies, *Biochem. J.*, 1955, **61**, 89.
[12] Murray and Cloke, *J. Amer. Chem. Soc.*, 1946, **68**, 126.
[13] Tafel and Stern, *Ber.*, 1900, **33**, 2224.
[14] Carter and Loo, *J. Biol. Chem.*, 1948, **174**, 723.
[15] Radhakrishnan and Meister, *Fed. Proc.*, 1956, **15**, 333; *J. Biol. Chem.*, 1957, **226**, 559; Witkop and Beiler, *J. Amer. Chem. Soc.*, 1956, **78**, 2882.

TABLE 1. *Periodate uptake (moles of periodate per mole of substance).*

Time of oxidn. (hr.)	Proline			Hydroxyproline			Histidine hydrochloride		*N*-Methylglycine
	NB *	pH 2·2	pH 10·2	NB *	pH 2·0	pH 8·5	NB *	pH 2·0	NB *
0·5	0·33	0·26	0·26	1·3	1·0	0·7	0·19	0·19	0·11
1	0·42	0·31	0·51	1·5	1·15	0·99	0·38	—	0·12
1·5	—	—	—	—	—	1·33	—	—	—
2·5	—	0·75	1·04	—	1·73	1·84	—	—	—
3	1·03	—	—	2·2	—	—	0·95	0·49	—
5·8	—	—	—	—	2·68	—	—	—	—
6·4	—	—	—	3·5	—	—	—	—	—
7·5	—	1·08	1·77	—	—	—	—	—	—
16·5	—	—	—	—	—	—	—	—	0·47
22	—	—	—	—	—	—	—	0·83	—
24	1·95	0·98	1·97	4·1	2·98	—	2·18	—	—
43	—	—	—	—	—	—	—	—	0·79
48	2·01	—	—	4·1	2·98	—	4·05	—	—
67	—	—	—	—	—	—	—	1·0	0·97
89	—	—	—	—	—	—	—	—	1·09
96	—	—	—	—	—	—	—	1·07	—

* NB = not buffered.

TABLE 2. *Carbon dioxide produced (moles of CO_2 per mole of substance).*

Time of oxidn. (hr.)	*N*-Methylglycine NB,* 37°	Proline		Hydroxyproline		
		NB * (25°)	In 0·2N-H_2SO_4 (25°)	NB * (20°)	In 0·01N-H_2SO_4 (25°)	NB * (37°)
0·25	—	0·18	0·04	0·20	0·13	—
0·5	0·07	0·28	0·08	0·39	0·31	—
1	0·13	0·48	0·16	0·63	0·55	—
1·5	0·16	—	—	0·80	—	—
2	0·18	0·66	0·29	0·95	0·79	—
2·5	0·19	—	—	—	0·83	—
3	0·22	0·77	—	1·17	—	—
3·5	0·26	—	—	—	0·89	—
4	0·33	0·83	0·50	1·25	—	1·9
4·5	0·38	—	—	—	0·93	—
5	—	—	0·61	1·33	0·95	1·9
6	—	—	0·66	1·36	—	—
7	—	—	0·71	1·39	0·95	—
13	—	0·99	—	—	—	—

* NB = not buffered.

for the determination of the periodate consumption [16] and in the case of unbuffered solution for the estimation of acid liberated.[2] Results are in Table 1.

Glycine, alanine, phenylalanine, *N*-acetylglycine, glycylglycine, glycylproline, pyrrolid-2-one, pyrrole-2-carboxylic acid and pyrrolidine did not react with sodium metaperiodate. Histidine hydrochloride yielded 0·27 equivalent of acid after oxidation for 48 hr.

N-Methylglycine (20 mg.), proline (0·36 mg.), and hydroxyproline (0·53 mg.) were separately oxidised with 0·03M-sodium metaperiodate (0·5 ml.), and the liberated carbon dioxide was determined in a Warburg apparatus [17] (see Table 2).

A solution of hydroxyproline (10 mg.) in 0·3M-sodium metaperiodate solution (6 ml.) was made up with water to 50 ml. and kept for 18 hr. in the dark. Aliquot portions (0·5 ml.) were removed and the ammonia contents determined by the Conway method.[18] After 18 hr., 0·44 mole of ammonia per mole of hydroxyproline was found.

An aqueous solution of hydroxyproline (0·53 mg.), 0·1N-*p*-hydroxybenzaldehyde (1 ml.), and 0·3M-sodium metaperiodate (2 ml.) was made up to 25 ml. and set aside for 17 hr. Aliquot portions (1 ml.) were taken for formaldehyde estimation by the chromotropic acid method.[19] After 17 hr., 0·83 mole of formaldehyde per mole of hydroxyproline was found. An oxidation was carried out at pH 2·0 for 15 hr.; after removal of periodate formaldehyde was absent as shown by Schryver's method (phenylhydrazine–ferricyanide reagents [20]). Another sample was

[16] Neumüller and Vasseur, *Arkiv Kemi, Min., Geol.*, 1953, **5**, 235.
[17] Dixon, "Manometric Methods," Cambridge University Press, 1953.
[18] Conway, "Micro-diffusion Analysis and Volumetric Error," Crosby Lockwood, London, 1950.
[19] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.
[20] Hough, Powell, and Woods, *J.*, 1956, 4799.

treated with a solution saturated with barium chloride and sodium hydrogen carbonate (4 : 1 respectively) to remove periodate,[20] and the filtrate kept at pH 7·5 for 17 hr.: formaldehyde was again absent.

Oxidation of Proline.—(1) *Characterisation of pyrroline.* An aqueous solution (30 ml.) of L-proline (0·25 g.) was mixed with 0·3M-sodium metaperiodate solution (7 ml.) and kept in the dark for 2·5 hr. After saturation with potassium carbonate, the solution was continuously extracted with ether for 24 hr. The ethereal extract was concentrated to *ca.* 5 ml., then mixed with ethanol (15 ml.) and Adams catalyst (135 mg.), and the mixture shaken in hydrogen for 8 hr. at room temperature and atmospheric pressure. Consumption of hydrogen by the catalyst being excluded, *ca.* 10 ml. of hydrogen were consumed during the reaction. The catalyst was filtered off, and the filtrate acidified with concentrated hydrochloric acid (1 ml.) and evaporated under reduced pressure to a syrup (170 mg.). The toluene-*p*-sulphonyl derivative was then prepared and crystallised from light petroleum–methanol as needles (22 mg.), m. p. and mixed m. p. with *N*-toluene-*p*-sulphonylpyrrolidine, 120° (Found: C, 58·9; H, 6·5; N, 5·6. Calc. for $C_{11}H_{15}O_2NS$: C, 58·7; H, 6·7; N, 6·2%).

0·3N-Sodium metaperiodate (35 ml.) was added to proline (0·5 g.) in sulphuric acid (pH 2·0; 40 ml.) and the mixture kept for 24 hr. in the dark. Excess of periodate was precipitated by the addition of a solution saturated with barium chloride and sodium hydrogen carbonate (4 : 1).[20] The filtrate was saturated with potassium carbonate and continuously extracted with ether for 24 hr. The ethereal extract was mixed with aqueous methanol and concentrated under reduced pressure to *ca.* 10 ml. The resulting aqueous solution was exactly neutralised (2N-hydrochloric acid), and an equal volume of saturated aqueous mercuric chloride solution was added: a white complex (*ca.* 75 mg.) was precipitated. After being washed with ethanol and ether, the product was dried (P_4O_{10}) under reduced pressure (Found: C, 13·5; H, 2·2; N, 3·4. Calc. for $C_4H_7NCl_2Hg$: C, 14·0; H, 2·1; N, 4·1%).

(2) *Characterisation of pyrrolid-2-one.* (*a*) Unbuffered solution. A mixture of L-proline (0·26 g.) in water (10 ml.) and 0·3M-sodium metaperiodate solution (30 ml.) was set aside for 24 hr. in the dark. An ether extract, prepared as above, was mixed with concentrated hydrochloric acid (1 ml.) and concentrated under reduced pressure. The residue was then evaporated several times with water (*ca.* 5 ml. portions) to remove excess of hydrochloric acid, and finally with methanol (10 ml.). The product (0·16 g.) was sublimed under reduced pressure at 100° to give white needles, m. p. 88°, which gave an *X*-ray powder photograph identical with that of authentic pyrrolid-2-one hydrochloride (Found: C, 46·0; H, 7·4; N, 13·2; Cl, 16·8. Calc. for $C_8H_{15}N_2O_2Cl$: C, 46·5; H, 7·3; N, 13·6; Cl, 17·2%).

A mixture of L-proline (0·25 g.) and 0·3M-sodium metaperiodate solution (30 ml.) was kept for 5 hr., and after near-saturation with potassium carbonate the solution was continuously extracted with ether. The ether extract was evaporated almost to dryness, then the residue was heated at 100° under reflux for 2·5 hr. with either 50% sulphuric acid (5 ml.) or concentrated hydrochloric acid (5 ml.). The neutralised solution (barium or silver carbonate respectively) was concentrated to a syrup (90 mg.) which readily crystallised, having m. p. and mixed m. p. with γ-aminobutyric acid, 195°. An *X*-ray powder photograph of the product was identical with that of an authentic specimen.

(*b*) At pH 10·2. A mixture of L-proline (0·25 g.), 0·1M-boric acid (10 ml.), 0·1N-sodium hydroxide (10 ml.), and 0·3M-sodium metaperiodate (30 ml.) was kept in the dark for 20 hr. Pyrrolid-2-one hydrochloride (0·21 g.) was isolated as above (Found: C, 46·6; H, 7·5; N, 13·8%).

(*c*) At pH 2·1. The above procedure when repeated with proline (0·25 g.) at pH 2·1 (adjusted with 0·01N-sulphuric acid) yielded a syrup which on sublimation gave pyrrolid-2-one hydrochloride (*ca.* 1 mg.).

Periodate–p-Anisidine Spray Reagents.—Substances reacting rapidly with sodium metaperiodate were detected by thinly spraying the chromatograms with 0·01M-sodium metaperiodate,[7,8] followed after 2 min. by *p*-ansidine or *p*-anisidine hydrochloride (1% solution in butan-1-ol). White spots on a pink background appeared within 1—2 min. if periodate-reacting substances were present. This method will detect polyols at a concentration of 25×10^{-6} g.

We thank Dr. T. Bevan for the *X*-ray powder photographs, Mr. M. D. Cantley for experimental assistance, and the Medical Research Council for an award (to P. D. B.).

THE UNIVERSITY, BRISTOL. [*Received, May 2nd,* 1958.]

815. *Submicro-methods for the Analysis of Organic Compounds. Part V.*[1] *The Determination of Sulphur.*

By R. Belcher, R. L. Bhasin, R. A. Shah, and T. S. West.

Sulphur in organic compounds can be determined by decomposing *ca.* 50 μg. samples with fuming nitric acid and anhydrous barium chloride at 275—280°. The precipitated barium sulphate is centrifuged off, washed, and dissolved in an excess of ammoniacal 0·02M-EDTA. The sulphur is determined indirectly by titration of the excess of chelating agent with standard 0·01M-magnesium chloride (screened Solochrome Black T indicator). Average results for any one compound are within 0·20%; no result is likely to exceed by 0·4% the absolute sulphur content.

Several methods are available for the decomposition of organic compounds in order to determine their sulphur content, *e.g.*, dry oxidation in a stream of oxygen or air, wet oxidation with, *e.g.*, nitric acid, and fusion with an alkali metal or alkali-metal peroxide. Previous experience of absorption of small amounts of material from gas streams led us to consider only the wet oxidation and the fusion methods.

Initially fusion with an alkali-metal was used as this had proved successful in the submicro-determination of bromine and iodine.[1] After fusion as in that work, the sulphide was oxidised by hydrogen peroxide or bromine and sulphate determined by (*a*) passage through an ion-exchange column (hydrogen form) and titration of the eluted sulphuric acid, or (*b*) precipitation as barium sulphate and complexometric titration with disodium ethylenediamine tetra-acetate (EDTA) to determine either the excess of barium chloride [2] or the precipitated barium salt.[3] Both procedures (*a*) and (*b*) were satisfactory when inorganic sulphate was used as the test material. The ion-exchange procedure was unsatisfactory for submicro-determination of sulphur in organic compounds because of the high control values obtained on the reagents. The most successful of the complexometric methods (*b*) was that involving determination of the precipitated barium. However, silicates leached from the glass tube during fusion with metallic sodium interfered. Interference was also observed when the glass tubes, hitherto used in this type of work, were replaced by small nickel bombs. In this instance, traces of nickel leached from the bombs caused replacement of the magnesium used as back-titrant from its EDTA chelate and reacted irreversibly with the hydroxyazo-dye used as indicator. Fusions with sodium peroxide were not practicable because of the impurity of the reagent and difficulties associated with high electrolyte concentration in the resulting solutions. A detailed account of these procedures has been given elsewhere.[4]

The method finally selected was to heat ~50 μg. of the sulphur compound with ~200 μg. of anhydrous barium chloride and 50 μl. of fuming nitric acid in a sealed glass tube at 275—280° for 7 hours, evaporate off the nitric acid, dissolve the soluble salts, collect the barium sulphate and dissolve it in a measured excess of EDTA in ammoniacal solution, and titrate the excess of chelating agent.

The results, shown in the Table, refer to substances of known purity (nos. 1—4) and others (nos. 5—9) supplied as unknowns by various workers in this Department. Not all these compounds are of theoretical composition, but in each instance the results obtained by the submicro-method are in close agreement with those obtained by normal organic microanalysis. Sample 10 (thiourea) was selected because of its high sulphur content and gave low results by this method; we attributed this to the presence of insufficient barium chloride, but subsequently found that the excess of EDTA necessary

[1] Part IV, Belcher, Shah, and West, *J.*, 1958, 2998.
[2] Belcher, Gibbons, and West, *Chem. and Ind.*, 1954, 850.
[3] *Idem, ibid.*, p. 127.
[4] Shah, Ph.D. Thesis, Birmingham, 1957.

to dissolve the increased amount of barium sulphate was the most important factor. When double the previous excess of EDTA was used no further trouble was experienced in this analysis.

Apart from the somewhat long decomposition time, the method is quite rapid. No attempt was made to reduce this time since generally decomposition was allowed to proceed overnight.

Compound	Range of wts. (μg.)	Sulphur (%) Calc.	Found	Error (%)	No. of Detns.	Range of errors (%) Max.	Min.
Sulphonal	49·96—59·53	28·09	28·03	0·06	3	−0·13	+0·04
Benzyl disulphide	50·01—61·08	26·03	26·12	0·09	3	+0·25	−0·05
Phenylthiourea	47·95—57·99	22·86	22·76	0·10	3	−0·19	+0·03
S-Benzylthiuronium chloride	52·67—58·34	15·82	15·71	0·11	3	−0·44	±0·00
1 : 4-Di-iodo-2 : 3-di-*o*-toluene-sulphonylbutane	50·60—69·88	9·86	9·76	0·10 †	4	−0·33	−0·11
Na octane-1-sulphonate	47·08—68·69	14·80—14·43 *	14·27	0·16 †	3	−0·42 †	+0·06 †
8-Hydroxy-7-iodoquinoline-5-sulphonic acid	43·33—68·42	9·11, 9·28 *	9·29	0·01 †	7	−0·12 †	+0·01 †
p-Bromo-*N*-*p*-methoxyphenyl-benzenesulphonamide	48·60—66·40	9·36, 9·36 *	9·38	0·02	4	+0·29	−0·04
$(HO_2C{\cdot}CH_2{\cdot}S{\cdot})_2$	47·89—48·33	30·47, 29·78 *	29·65	0·13	4	−0·32 †	+0·07 †
Thiourea	47·15—59·98	42·12	42·04	0·08	4	−0·16	+0·04

* Actual analyses by routine micromethod. † Difference from microanalytical result.

In the method we recommend, it is important to use nitric acid of optimum strength (*d* 1·5): incomplete recoveries are obtained with weaker acid. It is also important to observe the recommended procedure for dissolution of the barium sulphate in ammoniacal EDTA. We have used the EDTA procedure on the macro-, the micro-, and the submicro-scale and find that it is relatively much more difficult to dissolve barium sulphate on the submicro-scale. The manner of precipitation of the barium sulphate in the Carius type of procedure may be responsible for this, as it is known that well-aged barium sulphate is considerably more difficult to dissolve than the freshly precipitated variety.

Experimental

Reagents.—(1) Fuming nitric acid (*d* 1·5) of "AnalaR" grade. (2) Anhydrous barium chloride, "AnalaR" dihydrated salt dehydrated at 200° for 6 hr. (3) 1 : 300 Hydrochloric acid, prepared from "AnalaR" reagent. (4) Solochrome Black T indicator, 0·1% ethanolic solution prepared daily. (5) Dimethyl Yellow, 0·05% solution in ethanol. (6) 0·02M-Disodium ethylenediaminetetra-acetate dihydrate, standardised against metallic magnesium. (7) 0·01M-Magnesium chloride, evaluated against standard 0·02M-EDTA. (8) Ammonia, "AnalaR" concentrated reagent. (9) Filter-paper pulp, prepared in the usual way from "Whatman" ashless paper.

Apparatus.—(1) Magnetic stirrer. (2) "Agla" micrometer syringe burettes. (3) 2-ml. hypodermic syringe. (4) Hypodermic needle, 1½″, 22 BWG. (5) Transference-pipette. (6) Heating block for Carius digestion, capable of holding 8 tubes at a temperature of 275—280°, electrically heated and controlled by a "Simmerstat." (7) Heating-block (130—135°) for digestion of precipitate with EDTA, similarly heated and controlled. (8) Digestion-tubes prepared from "Pyrex" (1·3 × 7·5 cm.) or "Phœnix Regina" (3″ × ½″) test-tubes, cleaned as described earlier.[5] (9) Cylindrical "dural" block bored to hold digestion tubes during cooling. (10) Submicro-filtration device.[1] (11) Semimicro-"Eureka" electric centrifuge. (12) Platinum tetrahedra, to promote smooth boiling. (13) Small glass-encased rotor for use with magnetic stirrer, which must function efficiently in the presence of the platinum tetrahedron.

Procedure.—A 50 μg. sample was weighed on a submicro-balance [6] and transferred to the

[5] Belcher, West, and Williams, *J.*, 1957, 4323. On p. 4326, line 6 from the bottom of the page, *for* potassium iodide *read* potassium bromide.

[6] Asbury, Belcher, and West, *Mikrochim. Acta*, 1956, 598.

bottom of a clean dry test-tube by tapping the tweezers holding the inverted platinum weighing-vessel gently against the edge of the tube. The tube itself was gently tapped to prevent the sample's adhering to the walls near the top of the tube. About 200 μg. of anhydrous barium chloride (approximately weighed on the submicro-balance) were then transferred to the bottom of the tube by the same procedure. 50 μl. of nitric acid (*d* 1·5) were delivered to the tube by means of a syringe burette, and the tubes were sealed near the open end.[5] Difficulty was sometimes experienced in sealing the tubes owing to the vapour pressure of the acid, but the procedure was simplified if the test-tube was drawn out near the end, cooled, and then sealed.

The sealed tubes were placed in the cold heating-block with just the tip protruding and the temperature was raised and kept at 275—280° overnight (or for at least 7 hr.). The heating-block was switched off and the tubes were removed when nearly cool. They were then centrifuged for 5 min. and the pressure in the tubes was released by heating the tip of each tube in a flame. The tubes were opened near the top in the usual way.[5]

The walls of each tube were washed down with 1 ml. of distilled water from a 2 ml. hypodermic syringe. The tubes were centrifuged once more for 1 min. and the contents evaporated to dryness in the heating-block, now adjusted to 100—110° by means of the Simmerstat control. 1 ml. of 1 : 300 hydrochloric acid was added to each tube and the temperature was kept at 90—100° for 30 min. The tubes were then removed from the heating-block and set aside for *ca.* 2 hr. after which they were centrifuged for a further 5 min. The supernatant liquid in each tube was next removed by means of a transference-pipette, care being taken to remove as little barium sulphate as possible, and filtered on the submicro-filtration apparatus through paper-pulp, under gentle suction. 1 ml. of 1 : 300 hydrochloric acid was again added to the tube which was then centrifuged for a further 5 min. The transference and filtration were repeated as before. The whole process was repeated with two 0·5 ml. lots of distilled water. Finally the pulp-pad was transferred back to the tube by means of a hypodermic needle. Washings from (1) the funnel, (2) the inside and outside of the transference pipette, and (3) the tip of the hypodermic needle (not more than 1·5 ml. in all) were then collected in the tube. Finally, 100 μl. of 0·02M-EDTA were added from a syringe burette, two drops of concentrated " AnalaR " ammonia, and a platinum tetrahedron. The mixtures were then brought to the b. p. during 4—5 min. by placing the tubes in the heating-block at 130—135°; boiling was maintained for a further 5 min. The tubes were removed and cooled, and the contents treated with a further drop of ammonia, brought to the b. p. once more (4—5 min.), and boiled for a further 5 min. The tubes were finally taken out of the heating-block, cooled, and centrifuged for 1 min. A small glass-encased iron rotor was added to each tube and the excess of EDTA was titrated with standard magnesium chloride from a syringe burette after addition of one drop each of Solochrome Black T, Dimethyl Yellow, and concentrated ammonia. The colour change at the end-point was from green to *just* red.

A control analysis carried out on the reagents was usually negligible.

For compounds of high sulphur content, *e.g.*, thiourea (S, 42·1%), a larger amount of anhydrous barium chloride should be used (250—300 μg.), and 200 μl. of 0·02M-EDTA for dissolution of the larger amount of barium sulphate involved.

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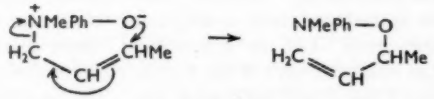
816. *The Rearrangement of Amine Oxides.*

By A. H. Wragg, T. S. Stevens, and D. M. Ostle.

Further evidence is provided that the Meisenheimer rearrangement of amine oxides to trisubstituted hydroxylamines is an intramolecular process independent of added alkali. Substituents in the amine oxides have in part their expected effect on the speed of rearrangement, showing a parallelism with the effect of the same substituents on the rearrangement of quaternary ammonium ions, but the "stationary groups" have an effect not easily understood.

The Meisenheimer rearrangement of amine oxides to *ONN*-trisubstituted hydroxylamines was examined in some detail by Cope and his collaborators,[1] who showed that but-2-enylmethylaniline oxide afforded *N*-methyl-*O*-1-methylallyl-*N*-phenylhydroxylamine, so that in this case at least the rearrangement appears to be intramolecular, proceeding by a cyclic mechanism:



They also effected the rearrangement, under slightly modified conditions, of amine oxides not containing an *N*-aryl group. It is a very important, though not quite a necessary, condition that the migrating radical be of allyl or benzyl type.

This rearrangement is comparable with that of phenacylammonium salts: $^{+}NRMe_2 \cdot CH_2 \cdot COPh \longrightarrow H^{+} + {}^{+}NRMe_2 \cdot {}^{-}CH \cdot COPh \longrightarrow NMe_2 \cdot CHR \cdot COPh$, in which an allyl, 1-phenylethyl, diphenylmethyl, or fluorenyl radical migrates much faster than benzyl, and the process is accelerated by electron-attracting *meta*- and *para*-substituents and by all *ortho*-substituents in a migrating benzyl radical. We have explored the recurrence of these relations in the amine oxide rearrangement by simple kinetic experiments, which also indicate that the process is of the first order in free amine oxide and independent of the presence of the alkali used in excess by Meisenheimer.

In the first series (Table 1) the oxides of benzylmethylaniline and analogous bases were isomerised in alcoholic solution, and the reaction followed at each stage by titrating the remaining oxide with titanous sulphate. Here, again, the allyl group migrates faster than

Table 1.

No.	Amine oxide	k_{10}	k_{30}	k_{60}
1	$Ph \cdot CH_2 \cdot N^{+}(O^{-})MePh$	—	—	0·0062
2	$Ph \cdot CH_2 \cdot {}^{+}N(O^{-})Me \cdot C_6H_4Br(p)$	—	—	0·014
3	$CH_2{=}CH \cdot CH_2 \cdot {}^{+}N(O^{-})MePh$	—	0·0071	—
4	$CH_2{=}CH \cdot CH_2 \cdot {}^{+}N(O^{-})Ph \cdot CH_2Ph$	0·013	0·055	—

benzyl (cases 1 and 3); in case 4, the allyl group migrates exclusively. Electron-attracting substituents in either of the "stationary" radicals should accelerate the reaction, which removes the positive formal charge of the nitrogen atom to which they are attached; this is the effect of the bromine substituent in case 2, and of the additional phenyl group in 4 as compared with 3.

While benzyl- and allyl-dialkylamine oxides rearrange with some reluctance and the production of by-products, dialkyldiphenylmethylamine oxides are transformed very smoothly, and variously substituted examples are relatively easy to prepare. In these cases the progress of rearrangement was followed by directly isolating the resulting trialkylhydroxylamines, and the results are set out in Table 2, which also contains for comparison the approximate basic dissociation constants (K_b) of the tertiary amines from which the

[1] Cope *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 1929; 1949, **71**, 3423, 3929.

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oxides are derived. In each of the series (*A*), (*B*), and (*C*), the velocity of rearrangement increases as the basic strength of the tertiary amine decreases; the effect of the electron-

TABLE 2. *Rearrangement of oxides* $^{-}O{\cdot}N^{+}RR'R''$.

No.	Migrating group, R		Stationary groups, R′, R″: Me_2 (*A*)	$-[CH_2]_5-$ (*B*)	$-[CH_2]_2{\cdot}O{\cdot}[CH_2]_2-$ (*C*)
5	Diphenylmethyl	10^3k	4·4	3·5	1·8
		$10^{10}K_b$	350	100	3·4
6	9-Fluorenyl	10^3k	5·3	5·1	3·5
		$10^{10}K_b$	210	21	3·0
7	Phenyl-*o*-tolylmethyl	10^3k	11·8	10·0	5·2
		$10^{10}K_b$	140	14	2·5
8	Di-*p*-nitrophenylmethyl	10^3k	200	—	—
		$10^{10}K_b$	1·4	—	—
9	Di-α-naphthylmethyl	10^3k	—	—	130
		$10^{10}K_b$	—	—	0·09

attracting nitro-groups is outstanding. *p*-Nitro- and *o*-methyl substituents have the same influence here as when introduced into a migrating benzyl group in the quaternary ammonium salt rearrangement. On the other hand, those changes in the stationary groups which increase the basic strength of the tertiary amines (horizontal series) *accelerate* the isomerisation, an effect not easily accounted for. The piperidine derivatives in this series are weaker bases than their dimethylamine analogues.

The intramolecular character of the transformation has been confirmed by effecting the rearrangement of a mixture of the oxides 7*A* and 9*C*. Here the separation of *NN*-dimethyl-*O*-phenyl-*o*-tolylmethylhydroxylamine and *N*-di-α-naphthylmethoxymorpholine was easy by steam-distillation; they were obtained in almost quantitative yield, and no other product could be recognised such as would arise from any process of fission and cross-recombination. Though the velocities of rearrangement of 7*A* and 9*C* are more disparate than would be desired in such an experiment, the excellent yields of pure materials show the reaction to be at least predominantly intramolecular.

The compounds listed in Table 1 were prepared by oxidising the tertiary bases with monoperphthalic acid, and the nature of the new products of rearrangement was confirmed by reductive fission: $NRR'{\cdot}OR'' \longrightarrow NHRR' + HOR''$. For the compounds in Table 2, perbenzoic acid was used in the oxidation, and most of the tertiary bases were prepared from the appropriate secondary amine and diarylmethyl bromide. In two cases the following route was used: $Ph{\cdot}CHO + NHMe_2 + HCN \longrightarrow H_2O + Ph{\cdot}CH(CN){\cdot}NMe_2$; $Ph{\cdot}CH(CN){\cdot}NMe_2 + ArMgBr \longrightarrow Ph{\cdot}CHAr{\cdot}NMe_2 + MgBrCN$.

Members of series 5, 6, and 7, having two ethyl groups as stationary groups, were prepared and their rearrangement effected, but they did not lend themselves to kinetic study.

EXPERIMENTAL

Compound 1.—Benzylmethylaniline (10 g.) in ether (50 ml.) was treated at 0° with ethereal monoperphthalic acid [2] (10% excess). After 16 hr., the supernatant ether was decanted, and dry hydrogen chloride passed into the syrup dissolved in dry chloroform. Phthalic acid was filtered off and the solvent was removed under reduced pressure below 50°. The residual syrupy benzylmethylaniline oxide hydrochloride, crystallised from ethanol–ether (yield 7·8 g.) and then from acetone, had m. p. 131° (lit.,[3] 135°). When heated in 10% sodium carbonate solution at 90° it gave *O*-benzyl-*N*-methyl-*N*-phenylhydroxylamine having the recorded [3] properties, together with appreciable quantities of benzaldehyde, recognised as 2 : 4-dinitrophenylhydrazone.

Compound 2.—*p*-Bromo-*N*-methylaniline [4] had b. p. 128—133°/9 mm.; the *picrate* crystallised from ethanol–acetone in needles, m. p. 172—173° (Found: C, 38·2; H, 2·6. $C_{13}H_{11}O_7N_4Br$

[2] Böhme, *Org. Synth.*, 1940, **20**, 70.
[3] Meisenheimer, Glawe, Greeske, Schorning, and Vieweg, *Annalen*, 1926, **449**, 188.
[4] Fries, *Annalen*, 1906, **346**, 173.

requires C, 37·6; H, 2·6%), and the *hydrochloride* from ethanol–ether in prisms, m. p. 135—136° (Found: C, 38·4; H, 4·0; Cl, 16·1. C_7H_9NClBr requires C, 37·8; H, 4·0; Cl, 16·0%). The base (4·65 g.) was heated at 95° for 1 hr. with allyl bromide (3·32 g.), and the basic material distilled. *N*-Allyl-*p*-bromo-*N*-methylaniline (4·76 g.) had b. p. 134—138°/6 mm., and gave a *picrate*, prisms, m. p. 136°, from ethanol–acetone (Found: C, 42·3; H, 3·3. $C_{16}H_{15}O_7N_4Br$ requires C, 42·2; H, 3·3%). Oxidation with perphthalic acid failed to give a crystalline amine oxide hydrochloride. Benzyl chloride (19·9 g.) and *p*-bromo-*N*-methylaniline (27·9 g.) were heated at 95° for 3 hr. Distillation of the basic material gave *N*-benzyl-*p*-bromo-*N*-methylaniline [5] (27 g.), b. p. 195—205°/9 mm.; the *picrate*, pale yellow prisms from ethanol–acetone, had m. p. 129—129·5° (Found: C, 47·1; H, 3·4. $C_{20}H_{17}O_7N_4Br$ requires C, 47·5; H, 3·4%).

Compound 3.—Allylmethylaniline [6] was oxidised as in case (1) and the oxide salt and hydroxylamine were obtained having the recorded [6] properties.

Compound 4.—Allylaniline, b. p. 100—110°/9 mm., was prepared in 60% yield by refluxing an alcoholic suspension of sodium formanilide with allyl bromide (10% excess) for 1 hr., giving crude allylformanilide, b. p. 145—150°/10 mm., which was hydrolysed by 16 hours' boiling with 20% alcoholic potassium hydroxide. It was converted by Wedekind's method [7] into *N*-allyl-*N*-benzylaniline, b. p. 173—180°/9 mm.; the *hydrochloride* crystallised from ethanol–ether in prisms, m. p. 138° (Found: C, 73·8; H, 6·6; Cl, 14·0. $C_{16}H_{18}NCl$ requires C, 74·0; H, 6·9; Cl, 13·7%); and the *picrate* crystallised from ethanol in prisms, m. p. 128° (Found: C, 58·5; H, 4·4; N, 12·3. $C_{22}H_{20}O_7N_4$ requires C, 58·4; H, 4·4; N, 12·4%). When less pure specimens of allylaniline were used, the product gave a crude hydrochloride, m. p. 207°; the derived picrate had m. p. 110°, undepressed on admixture with *benzylaniline picrate*, which separated from ether as a microcrystalline powder, m. p. 113° (Found: C, 55·0; H, 3·9; N, 13·3. $C_{19}H_{16}O_7N_4$ requires C, 55·3; H, 3·9; N, 13·6%). Wedekind [7] records for allylbenzylaniline hydrochloride: m. p. 220—221°; Cl, 14·97 [calc. 14·46% (*sic*)]. Jones [8] stated that the hydrochloride had the properties described by Wedekind and that analyses (unquoted) corresponded with the formula $C_{16}H_{17}N,HCl$.

Compound 4 * (*Table* 3): *N-Methyl-N-1-phenylethylaniline*.—Methylaniline (32 g.) and 1-phenylethyl chloride (43·8 g.) were heated together at 95° for 20 hr. Distillation of the basic material gave *N*-methyl-*N*-1-phenylethylaniline (50·8 g.), b. p. 158—165°/7 mm. [*picrate*, prisms, m. p. 131°, from ethanol (Found: C, 57·6; H, 4·6. $C_{21}H_{20}O_7N_4$ requires C, 57·3; H, 4·5%); *hydrochloride*, prisms, m. p. 162°, from ethanol–ether (Found: C, 72·5; H, 6·9; N, 5·8; Cl, 14·5. $C_{15}H_{18}NCl$ requires C, 72·7; H, 7·3; N, 5·7; Cl, 14·3%)].

Compound 5*A*.—Potassium cyanide (33 g.) in water (200 ml.) was slowly added, with cooling, to benzaldehyde (53 g.) and dimethylamine hydrochloride (50 g.) in water (300 ml.) and methanol (100 ml.). After 2 hours' shaking, α-dimethylamino-α-phenylacetonitrile was extracted with ligroin, dried, and distilled (yield 69 g.; b. p. 120—125°/12 mm.). The nitrile (40 g.), in ether (100 ml.), was slowly added to phenylmagnesium bromide [from bromobenzene (78·5 g.), magnesium (12 g.), and ether (300 ml.)]. After 12 hr., ice and ammonium chloride were added, and the ethereal layer was concentrated and shaken with 10N-hydrochloric acid; the precipitated hydrochloride yielded diphenylmethyldimethylamine [9] (35 g.).

Compound 5*B*.—Diphenylmethyl bromide [10] (20 g.) and piperidine (20 g.) were refluxed for 1 hr. in benzene (50 ml.). The filtrate from piperidine hydrobromide was freed from benzene and piperidine by evaporation under reduced pressure, and treated with ether and 2N-sodium hydroxide. The ether layer gave, with 8N-hydrochloric acid, *N*-diphenylmethylpiperidine hydrochloride, m. p. 252° (Found: Cl, 12·3. Calc. for $C_{18}H_{22}NCl$: Cl, 12·3%). The free base (17·5 g.) crystallised from methanol in needles,[11] m. p. 77° (Found: C, 86·1; H, 8·4. Calc. for $C_{18}H_{21}N$: C, 86·1; H, 8·3%).

Compound 5*C*.—*N-Diphenylmethylmorpholine*, prepared from diphenylmethyl bromide and morpholine as in case 5B, crystallised from methanol in prisms, m. p. 74° (Found: C, 80·2; H, 7·5. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5%). The *hydrochloride* formed prisms, m. p. 239°, from ethanol (Found: Cl, 12·1. $C_{17}H_{20}ONCl$ requires Cl, 12·3%).

[5] Cf. Everatt, *J.*, 1908, **93**, 1236.
[6] Meisenheimer, *Ber.*, 1919, **52**, 1667.
[7] Wedekind, *Ber.*, 1899, **32**, 521; 1903, **36**, 3791 footnote.
[8] Jones, *J.*, 1905, **87**, 1722.
[9] Stevens, Cowan, and MacKinnon, *J.*, 1931, 2568.
[10] Courtot, *Ann. Chim.* (*France*), 1916, **5**, 80.
[11] Christiaen, *Bull. Soc. chim. belges*, 1924, **33**, 483.

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Compound 5 ** (Tables 3 and 4).—Analogously diphenylmethyldiethylamine was prepared from diphenylmethyl bromide (10 g.) and diethylamine (6·5 g.) in nitromethane (25 ml.). After 20 min. at 95°, the cooled mixture was treated with ether and 5N-sodium hydroxide (heat evolved). The free base crystallised from methanol in prisms,[12] m. p. 58—59°.

Compound 6*A*.—Bromine (9 g.) in carbon tetrachloride (30 ml.) was added gradually to fluorene (8·3 g.) and dibenzoyl peroxide (0·5 g.) in boiling carbon tetrachloride (100 ml.). The mixture was refluxed for 30 min. after evolution of hydrogen bromide had ceased; the solvent was removed under reduced pressure, and the residue, dissolved in ether, was washed with sodium hydrogen carbonate solution and dried.[13] Crystallisation from ligroin gave 9-fluorenyl bromide (8·5 g.), m. p 103°. It yielded 9-fluorenyldimethylamine [14] [*hydrochloride*, needles, m. p. 235° (decomp.), from ethanol (Found: Cl, 14·3. $C_{15}H_{16}NCl$ requires Cl, 14·5%)].

Compound 6*B*.—Piperidine (5 ml.) and 9-bromofluorene (5 g.) reacted in the same way as in case 5B. The benzene solution was diluted with ether, washed with alkali, and evaporated. Crystallisation from methanol gave 9-fluorenylpiperidine [15] (4·5 g.), m. p. 97° (Found: C, 86·4; H, 7·5; N, 5·3. Calc. for $C_{18}H_{19}N$: C, 86·7; H, 7·6; N, 5·6%) [*hydrochloride*, prisms, m. p. 249°, from ethanol (Found: Cl, 12·7. $C_{18}H_{20}NCl$ requires Cl, 12·4%)].

Compound 6*C*. *N*-9-Fluorenylmorpholine,[16] prepared in the same way, formed plates, m. p. 150°, from acetone–ethanol (Found: C, 81·3; H, 6·5; N, 5·6. Calc. for $C_{17}H_{17}ON$: C, 81·3; H, 6·8; N, 5·6%) [*hydrochloride*, needles, m. p. 158° (decomp.), from methanol (Found: Cl, 12·5. $C_{17}H_{18}ONCl$ requires Cl, 12·3%)].

Compound 6 ** (Tables 3 and 4).—*Diethyl-9-fluorenylamine*, prepared substantially as diphenylmethyldiethylamine, in 85% yield, was a slightly yellow oil, b. p. 188°/14 mm. (Found: N, 5·5. $C_{17}H_{19}N$ requires N, 5·9%). The *hydrochloride* crystallised from ethanol in plates, m. p. 197—199° (Found: Cl, 12·7. $C_{17}H_{20}NCl$ requires Cl, 13·0%).

Compound 7*A*. *Dimethyl(phenyl-o-tolylmethyl)amine* was prepared by adding α-dimethylamino-α-phenylacetonitrile (25 g.) in ether (40 ml) to the Grignard reagent from *o*-bromotoluene (38 g), magnesium (5·5 g.), and ether (150 ml.), and refluxing the whole for ½ hr. after 48 hr. at room temperature. The base (22 g.), isolated as in case 5*A*, crystallised from methanol in prisms, m. p. 46° (Found: C, 85·1; H, 8·4; N, 6·4. $C_{16}H_{19}N$ requires C, 85·3; H, 8·4; N, 6·2%) [*hydrochloride*, needles, m. p. 273° (decomp.), from methanol (Found: Cl, 13·2. $C_{16}H_{20}NCl$ requires Cl, 13·5%)].

Compound 7*B*.—Phenyl-*o*-tolylmethanol (5 g.) was refluxed with 48% hydrobromic acid (20 ml.) for 5 min., distilled up to 126°, and refluxed for 15 min. more.[10] The ether-soluble material, washed with aqueous sodium hydrogen carbonate, was dried and distilled, giving *phenyl-o-tolylmethyl bromide* (5·45 g.), b. p. 200°/14 mm. (Found: Br, 30·3. $C_{14}H_{13}Br$ requires Br, 30·6%). As in case 5*B* it yielded *N-phenyl-o-tolylmethylpiperidine*, b. p. 113°/0·2 mm. (Found: N, 5·1. $C_{19}H_{23}N$ requires N, 5·3%); the *hydrochloride* crystallised from ethanol in plates, m. p. 258° (Found: Cl, 12·0. $C_{19}H_{24}NCl$ requires Cl, 11·8%).

Compound 7*C*.—*N-Phenyl-o-tolylmethylmorpholine*, prepared as in case 5*B*, was a viscous oil, b. p. 144°/0·4 mm. (Found: N, 5·0. $C_{18}H_{21}ON$ requires N, 5·2%); the *hydrochloride* formed needles, m. p. 264° (decomp.), from ethanol (Found: Cl, 11·8. $C_{18}H_{22}ONCl$ requires Cl, 11·7%).

Compound 7 ** (Tables 3 and 4).—Phenyl-*o*-tolylmethyl bromide (5·45 g.) reacted with diethylamine (7 ml.) in nitromethane (20 ml.) as in the preparation of diphenylmethyldiethylamine. Distillation of the basic reaction product gave *diethyl(phenyl-o-tolylmethyl)amine* (4·55 g.), b. p. 177°/15 mm. (Found: N, 5·5 $C_{18}H_{23}N$ requires N, 5·5%). The *hydrochloride* crystallised from ethanol in prisms, m. p. 229° (Found: Cl, 12·1. $C_{18}H_{24}NCl$ requires Cl, 12·2%).

Compound 8*A*.—Molten diphenylmethane (40 g.) was added during ½ hr. to ice-cooled nitric acid (140 ml.; *d* 1·5) kept between 20° and 25°. After 15 min. at room temperature the mixture was cooled in ice until it crystallised, and poured into water (1 l.). The solid was washed successively with water, sodium hydrogen carbonate solution, alcohol, and ether, boiled with ether, filtered off, and crystallised from benzene with rejection of sparingly soluble material. The 4 : 4′-dinitrodiphenylmethane (20 g.; m. p. 183—184°) so obtained was refluxed in carbon

[12] Sommelet, *Compt. rend.*, 1922, **175**, 1150.
[13] Cf. Wittig and Vidal, *Chem. Ber.*, 1948, **81**, 368.
[14] Wittig and Nagel, *ibid.*, 1950, **83**, 106.
[15] Pinck and Hilbert, *J. Amer. Chem. Soc.*, 1946, **68**, 377.
[16] Cf. Bamford and Stevens, *J.*, 1952, 4675.

tetrachloride (300 ml.) with dibenzoyl peroxide (1·1 g.); then bromine (4 ml.) in carbon tetrachloride (20 ml.) was added. Within 30 min. evolution of hydrogen bromide ceased and the solid dissolved; after removal of the solvent, the residue was crystallised from acetone–ligroin and from carbon tetrachloride, giving **4 : 4′-*dinitrodiphenylmethyl bromide*** (22·5 g.), prisms, m. p. 90·5° (Found: N, 8·3. $C_{13}H_9O_4N_2Br$ requires N, 8·3%). This bromide (33·2 g.) in pure, dry nitromethane, was treated at −15° with anhydrous dimethylamine (13 g.) in nitromethane (100 ml.), and the deep red solution kept at 0° for 6 days. The solid (**4 : 4′-*dinitrodiphenylmethyl*)*dimethylamine*** crystallised from benzene–ethanol in needles (18 g.), m. p. 158—159° (Found: C, 59·6; H, 5·1; N, 13·7. $C_{15}H_{15}O_4N_3$ requires C, 59·8; H, 5·0; N, 13·9%). The ***hydrochloride***, prepared in acetone–ether, crystallised from methanol–ethanol in needles, m. p. 242° (decomp.) (Found: Cl, 10·2. $C_{15}H_{16}O_4N_3Cl$ requires Cl, 10·5%). When the preparation was carried out in ether–benzene, the main, non-basic product crystallised from benzene in needles, m. p. 299°, apparently solvated ***tetra*-p-*nitrophenylethylene*** (Found: C, 64·8; H, 3·8; N, 9·9. $C_{26}H_{16}O_8N_4,C_6H_6$ requires C, 65·1; H, 3·7; N, 9·5%).

Compound 9*C*.—Bromodi-α-naphthylmethane [17] (15 g.) was refluxed for 1 hr. with benzene (20 ml.) and morpholine (19 ml.). After addition of water and ether, the separated organic layer was shaken with 6N-hydrochloric acid. The precipitated hydrochloride yielded ***N*-di-α-*naphthylmethylmorpholine*** (18·5 g.), m. p. 174° after crystallisation from benzene–ligroin (Found: C, 84·9; H, 6·6; N, 4·1. $C_{25}H_{23}ON$ requires C, 85·0; H, 6·5; N, 4·0%).

Amine Oxide Salts.—Those containing an aryl group directly attached to nitrogen were prepared in the same way as in case **1** above. Allylmethylaniline oxide hydrochloride solution [6] was evaporated in a desiccator; the residue solidified after 9 weeks. Of the dialkyldiarylmethylamine oxide *salts* listed in Table 3, those containing two *N*-methyl groups were prepared

TABLE 3. *Amine oxide salts.*

					Found (%)				Required (%)		
No.	Salt	Form	Solvent	M. p.	C	H	N	Formula	C	H	N
2	Hydrochloride	Prisms	EtOH–Et_2O	122°	(HCl, 11·0)			$C_{14}H_{15}ONBrCl$	(HCl, 11·1)		
	Picrate	—	EtOH–$COMe_2$	125—126	46·4	3·4	10·4	$C_{20}H_{17}O_8N_4Br$	46·1	3·3	10·7
4	Hydrochloride	Prisms	EtOH–Et_2O	118	(HCl, 13·6)			$C_{16}H_{18}ONCl$	(HCl, 13·2)		
	Picrate	Prisms	EtOH	119—121	56·9	4·5	12·4	$C_{22}H_{20}O_8N_4$	56·4	4·3	12·0
4*	Picrate	Prisms	EtOH–$COMe_2$	126—128	55·6	4·6	12·4	$C_{21}H_{20}O_8N_4$	55·3	4·4	12·3
5*A*	Benzoate	Needles	$COMe_2$–Et_2O	108	—	—	3·9	$C_{23}H_{23}O_2N$	—	—	4·0
	Picrate	Needles	EtOH	158	55·7	4·4	12·1	$C_{21}H_{20}O_8N_4$	55·3	4·4	12·3
5*B*	Picrate	Plates	MeOH–$COMe_2$	166	57·8	4·5	—	$C_{24}H_{24}O_8N_4$	58·1	4·8	—
5*C*	Picrate	Needles	$COMe_2$	168—169	55·7	4·1	—	$C_{23}H_{22}O_8N_4$	55·7	4·4	—
5**	Picrate	Needles	EtOH–$COMe_2$	141	57·4	5·0	11·2	$C_{23}H_{24}O_8N_4$	57·0	5·0	11·6
6*A*	Benzoate	Needles	$COMe_2$–Et_2O	103	—	—	4·2	$C_{23}H_{21}O_2N$	—	—	4·0
	Picrate	Prisms	$COMe_2$	167	—	—	12·3	$C_{21}H_{18}O_8N_4$	—	—	12·3
6*B*	Picrate	Rhombs	EtOH–$COMe_2$	183	58·6	4·5	11·3	$C_{24}H_{22}O_8N_4$	58·3	4·5	11·3
6*C*	Picrate	Plates	EtOH–$COMe_2$	187	55·7	4·2	11·0	$C_{23}H_{20}O_8N_4$	55·7	4·0	11·3
6**	Picrate	Prisms	MeOH–EtOH	152	57·5	4·7	11·2	$C_{23}H_{22}O_8N_4$	57·3	4·6	11·6
7*A*	Benzoate	Needles	$COMe_2$–Et_2O	103	—	—	3·7	$C_{23}H_{23}O_2N$	—	—	3·9
	Picrate	Prisms	EtOH	130	56·3	4·7	11·7	$C_{22}H_{22}O_8N_4$	56·2	4·7	11·9
7*B*	Picrate	Needles	EtOH–$COMe_2$	153	58·7	5·2	11·2	$C_{25}H_{26}O_8N_4$	58·9	5·1	11·0
7*C*	Picrate	Needles	$COMe_2$–dioxan	173	55·9	4·8	11·0	$C_{24}H_{24}O_8N_4$	56·2	4·7	10·9
7**	Picrate	Prisms	EtOH–$COMe_2$	130	57·7	5·2	11·3	$C_{24}H_{24}O_8N_4$	57·9	5·2	11·3
8*A*	Picrate	Prisms	$COMe_2$	154	—	—	15·3	$C_{21}H_{18}O_{12}N_6$	—	—	15·4
9*C*	Hydrochloride	—	$CHCl_3$–Et_2O	150	(Cl, 8·8)		3·2	$C_{25}H_{24}O_2NCl$	(Cl, 8·8)		3·2

* *N*-Methyl-*N*-1-phenylethylaniline oxide; did not rearrange smoothly.

thus: diphenylmethyldimethylamine (10 g.) in dry toluene (75 ml.) was slowly added to a solution of perbenzoic acid (6·7 g.) in toluene (120 ml.) kept at 2°. After 10 min., precipitation was completed by addition of ligroin, and the solid, washed with ligroin and a little ether, yielded 14·6 g. of pure diphenylmethyldimethylamine oxide benzoate, which with ethanolic picric acid gave the picrate. In the other cases, with two exceptions (below), ether was added after the reaction was complete and the solution extracted repeatedly with N-hydrochloric acid; aqueous picric acid then precipitated the amine oxide picrate.

[17] Tschitschibabin, *Ber.*, 1911, **44**, 443.

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4 : 4′-Dinitrodiphenylmethyldimethylamine (5 g.) in toluene (130 ml.) was added dropwise to perbenzoic acid (3 g.) in toluene (50 ml.) kept below 0°. Precipitation of gummy solid was completed by adding chilled ligroin (250 ml.), and the gum, washed with ether, was dissolved in a minimum of cold acetone. Concentrated hydrochloric acid (10 ml.) was added at 0° and the mixture shaken with ether and sufficient water to dissolve the amine oxide hydrochloride. Picric acid then precipitated the oxide picrate from the aqueous layer.

Di-α-naphthylmethylmorpholine (4 g.) in toluene (60 ml.) was treated at −10° with perbenzoic acid (2·5 g.) in toluene (150 ml.). Precipitation was completed by addition of cold ligroin, and the gummy product was washed with ether and dissolved in ice-cold acetone. The amine oxide hydrochloride was precipitated by adding a solution of hydrogen chloride in acetone, followed by ether.

Trisubstituted Hydroxylamines.—The amine oxide salts (benzoates, picrates, or hydrochlorides) dissolved easily in 1% aqueous ammonia, and were rearranged by heating these solutions at 90—95° for the periods stated in Table 4, where the properties of the hydroxylamines are collected. In all cases in which the m. p. of the picrate of a hydroxylamine was near that of the parent amine oxide, a mixed m. p. showed a marked depression. To establish the constitution of the hydroxylamine from allylbenzylaniline oxide, this product (1·79 g.) in acetic acid (30 ml.) was reduced with zinc dust (7 g.) for 1·5 hr. at 95°. By ether-extraction after basification the mixture gave an oil (1·20 g.), b. p. 303—306°, which afforded benzylaniline picrate (mixed m. p.). In the same way the hydroxylamine from *N*-benzyl-*p*-bromo-*N*-methylaniline gave *p*-bromo-*N*-methylaniline, identified as picrate, in good yield.

TABLE 4. *Trisubstituted hydroxylamines.*

Case	Description	Found (%) C	H	N	Formula	Required (%) C	H	N	Heating (hr.)
2	Base (b. p. 102—107°/0·02 mm.)	58·4	4·8	4·8[a]	$C_{14}H_{14}ONBr$	57·6	4·8	4·8[c]	[a]
4	Base (b. p. 86—91°/0·04 mm.)	80·3	7·6	5·8	$C_{16}H_{17}ON$	80·3	7·2	5·8	[a]
5A	Base (b. p. 164°/16 mm.)	—	—	6·0	$C_{16}H_{17}ON$	—	—	6·2	3
	Picrate, plates (EtOH), m. p. 153°	—	—	12·3	$C_{21}H_{20}O_8N_4$	—	—	12·3	
5B	Base (b. p. 70°/0·2 mm.)	—	—	5·0	$C_{16}H_{21}ON$	—	—	5·2	16
	Picrolonate, needles (EtOH), m. p. 153°	63·0	5·2	—	$C_{28}H_{29}O_8N_5$	63·3	5·5	—	
5C	Base (b. p. 60°/0·2 mm.)	—	—	4·9	$C_{17}H_{19}O_2N$	—	—	5·2	18[b]
	Picrolonate, needles (EtOH), m. p. 141°	60·5	5·2	—	$C_{27}H_{27}O_7N_5$	60·8	5·1	—	
5**	Base (b. p. 120°/0·4 mm.)	—	—	5·5	$C_{17}H_{21}ON$	—	—	5·5	3
	Picrate, needles, (EtOH), m. p. 129°	57·4	5·0	11·5	$C_{23}H_{24}O_8N_4$	57·0	5·0	11·6	
6A	Base (b. p. 160°/13 mm.)	—	—	6·2	$C_{15}H_{15}ON$	—	—	6·2	2
	Picrate, needles (EtOH), m. p. 163—164°	55·7	4·1	—	$C_{21}H_{18}O_8N_4$	55·5	4·0	—	
	Picrolonate, needles (EtOH), m. p. 140°	—	—	14·2	$C_{25}H_{23}O_8N_5$	—	—	14·3	
6B	Base (b. p. 100°/0·15 mm.)	—	—	5·1	$C_{15}H_{19}ON$	—	—	5·3	5[b]
	Picrate, needles (EtOH), m. p. 132°	58·1	4·4	10·9	$C_{24}H_{22}O_8N_4$	58·3	4·5	11·3	
6C	Base, needles (EtOH), m. p. 162—163°	76·5	6·3	5·1	$C_{17}H_{17}O_2N$	76·4	6·4	5·2	4
6**	Base (b. p. 114°/0·2 mm.)	—	—	5·4	$C_{17}H_{19}ON$	—	—	5·5	4½[b]
	Picrate, plates (EtOH–$COMe_2$), m. p. 143°	57·5	4·6	11·3	$C_{23}H_{22}O_8N_4$	57·3	4·6	11·6	
7A	Base (b. p. 110°/0·2 mm.	—	—	5·6	$C_{16}H_{19}ON$	—	—	5·8	3
	Picrate, needles (MeOH), m. p. 140° ...	55·6	4·7	11·8	$C_{22}H_{22}O_8N_4$	56·2	4·7	11·9	
7B	Base (b. p. 126°/0·4 mm.)	—	—	4·8	$C_{19}H_{23}ON$	—	—	5·0	5[b]
	Picrate, needles (EtOH), m. p. 133°	59·1	5·1	11·1	$C_{25}H_{26}O_8N_4$	58·9	5·1	11·0	
7C	Base (b. p. 135°/0·4 mm.)	—	—	4·7	$C_{18}H_{21}O_2N$	—	—	4·9	5
	Picrate, prisms (EtOH), m. p. 128°	56·1	4·9	11·0	$C_{24}H_{24}O_8N_4$	56·2	4·7	10·9	
7**	Base (b. p. 113°/0·2 mm.)	—	—	4·9	$C_{19}H_{23}ON$	—	—	5·2	3½[b]
	Picrate, plates (EtOH), m. p. 139°	58·1	5·2	11·3	$C_{24}H_{26}O_8N_4$	57·9	5·2	11·2	
8A	Base, needles (EtOH–$CHCl_3$), m. p. 154—155°	56·6	4·7	—	$C_{15}H_{15}O_2N_3$	56·8	4·7	—	½
9C	Base, needles (EtOH–$CHCl_3$), m. p. 183°	81·3	6·2	3·8	$C_{25}H_{23}O_2N$	81·3	6·2	3·8	½

[a] Steam-distilled from sodium carbonate solution. [b] Isomerised in 70% ethanol. [c] Found: Br, 27·1. Required Br, 27·3%.

Kinetic Experiments.—Cases 1—4. The amine oxide hydrochloride in 99·7% alcohol, and alcoholic sodium ethoxide, were separately brought to the required temperature and mixed. Successive portions of 10 ml. were added to 0·5N sulphuric acid and 5 ml. of ligroin (which dissolves the hydroxylamine but not the amine oxide(, and made up with acid to 50 ml. The

unchanged oxide was determined in duplicate by boiling 20 ml. portions of the aqueous layer for 4 min. with a known excess of 0·05M-titanous sulphate and back-titration with 0·05N-iron alum solution in presence of thiocyanate. The apparatus was that of Thornton and Wood.[18] Allowance was made for a loss of 1·4% in the strength of titanous sulphate solutions boiled for 4 min. in control experiments. The hydroxylamines produced by rearrangement reduced less than 0·02 of an equivalent of titanous sulphate under the same conditions.

In a typical experiment, benzylmethylaniline oxide hydrochloride (0·8 g.) in 100 ml. of solution containing sodium ethoxide (1 mol.) reacted at 60° with the following results:

Time (min.)	0	46	110	150	195	240	288
Unchanged oxide [ml. of $Ti_2(SO_4)_3$]	16·78	13·43	7·88	6·31	5·15	3·69	3·08
k_1 (min.)	—	0·0048	0·0069	0·0065	0·0061	0·0063	0·0059

A run in which the sodium ethoxide concentration was doubled gave the mean constant 0·0060, and one in which both concentrations were halved gave 0·0062. The rearrangement is thus of the first order in amine oxide, and unaffected by alkali in excess of that used to liberate the base from its hydrochloride. Runs with the other oxides of this series were conducted in the same way as the typical experiment.

Cases 5A—9C. A preliminary run with diphenylmethyldimethylamine oxide benzoate in 1% aqueous ammonia, followed up to 72% conversion, showed that the reaction velocity *increased* with time. This may be accounted for by the separation of the insoluble liquid *O*-diphenylmethyl-*NN*-dimethylhydroxylamine, in which solvent of low dielectric constant the isomerisation of remaining amine oxide would be faster than in water. The solvent used in subsequent experiments was ethanol–water (7 : 3 by weight). The weighed amine oxide salt with the required amount of solvent was brought to the thermostat temperature (45° ± 0·1°), and an equal volume of solvent containing 1% of ammonia, at the same temperature, added; any solid salt dissolving at once on mixing. The final amine oxide solution was 0·071M, usually 30—50 ml. Reaction was stopped by chilling in acetone–carbon dioxide, and the mixture was transferred, with *ca.* 60 ml. of water and 60 ml. of ligroin (b. p. 40—50°), to a separating funnel. The water layer was washed with ligroin (2 × 30 ml.) and the combined ligroin extracts were washed with 0·5% aqueous ammonia (2 × 30 ml.) and water (50 ml.). These extracts were dried (K_2CO_3) and brought to constant weight in a vacuum. This hydroxylamine afforded the pure picrate or picrolonate in almost quantitative yield. In cases 8*A* and 9*C*, the chilled reaction mixture was diluted with water and the crystalline hydroxylamine filtered off through a Gooch crucible, washed, and dried to constant weight. When the united aqueous layers from which the hydroxylamine had been removed were acidified, with addition of picric acid if the original salt was not the picrate, unchanged amine oxide was precipitated quantitatively as picrate, which was collected after several hours at 0° and examined for purity, its complete solubility in 1% aqueous ammonia showing absence of the picrate of the hydroxylamine. This analytical separation was tested on known mixtures in each case, with 97—99% recovery. A typical series, with diphenylmethyldimethylamine oxide benzoate, gave the results:

Time of heating (min.)	20	30	60	125	150
Benzoate taken (g.)	0·7286	0·6646	0·8094	0·7951	0·5941
Hydroxylamine formed (g.)	0·0430	0·0588	0·1204	0·2032	0·1785
k_1 (sec.$^{-1}$)	0·0048	0·0049	0·0044	0·0040	0·0041

A series in which the amine oxide picrate was used, at twice the normal dilution, gave the same average value of k_1 0·0044. In cases 6*A* and 7*A* both benzoate and picrate were used, with similarly concordant results; 9*C* was studied as the hydrochloride, and in the other cases the picrate only was used.

The approximate K_b values for the tertiary bases were determined in the usual manner from the pH–neutralisation curves of the hydrochlorides with sodium hydroxide in dioxan–water (1 : 1 by volume).

Mixing Experiments.—*N*-Di-α-naphthylmethylmorpholine oxide hydrochloride (0·408 g.) and phenyl-*o*-tolylmethyldimethylamine oxide benzoate (0·400 g.) in ethanol (18 ml.) and water (6 ml.) with aqueous ammonia (0·5 ml.; *d* 0·880) were heated at 45° for 1 hr. and refluxed for 30 min. After addition of water the mixture was distilled exhaustively in steam. The ether extract (2 × 60 ml.) of the distillate was dried (Na_2SO_4) and evaporated, and the residue brought

[18] Thornton and Wood, *Ind. Eng. Chem.*, 1927, **19**, 150.

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to constant weight (0·2953 g., 97·7%) in a vacuum. This *NN*-dimethyl-*O*-phenyl-*o*-tolylmethylhydroxylamine gave 0·4970 g. (98·3%) of picrate, m. p. and mixed m. p. 139—140°, which depressed the m. p. of *N*-phenyl-*o*-tolylmethoxymorpholine picrate to 118—120°. The non-volatile material from the rearrangement was extracted with chloroform (2 × 50 ml.); the extract was evaporated and the residue dried to constant weight (0·3670 g., 98·9%). This product melted at 179°, and crystallisation from ethanol–chloroform gave *N*-di-α-naphthylmethoxymorpholine (0·3502 g.), m. p. and mixd m. p. 183°.

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817. *The Alkaline Hydrolysis of Nuclear-substituted Ethyl Cinnamates. The Cumulative Effects of Substituents.*

By Brynmor Jones and J. G. Watkinson.

Rates of hydrolysis of ethyl cinnamate and 28 nuclear-substituted derivatives with one, two, or three substituents have been measured at 24·8° in aqueous ethanol (85·4% of ethanol w/w). Additional measurements at other temperatures show that with the introduction of substituents, even into the *ortho*-position, the non-exponential factor of the Arrhenius equation does not vary beyond the limits of experimental error.

The cumulative effects of substituents indicate that when two substituents occupy the 2- and 4- or 3- and 5-positions their combined effect on the energy of activation is normally close to the sum of their individual effects. For other orientations, while the effects are sometimes approximately additive, there are often significant, and sometimes large, deviations from additivity.

In a previous paper [1] the cumulative effects of substituents on the alkaline hydrolysis of ethyl benzoate were studied because earlier results [2,3] had led to the belief that substituents in a benzene nucleus could contribute independent and additive increments to the energy of activation of reactions of the molecule in which they occur. There was also evidence of an analogous additivity of substituent effects on equilibria.[4] Agreement between the observed increments in energy of activation due to the substituents and values predicted on an additive basis was usually found [1] for 3 : 5-disubstitution; for 3 : 4-disubstitution substituent effects were approximately additive in some cases, but not in others. In the one case of trisubstitution (3 : 4 : 5-trimethoxy) investigated, the substituent effects were far from additive.

Other orientations of substituents were not examined because Ingold and Nathan,[5] Evans, Gordon, and Watson,[6] and Tommila and Hinshelwood [7] had shown that *ortho*-substituents in ethyl benzoate influence the non-exponential (entropy) factor of the Arrhenius equation as well as the energy of activation. *meta*- and *para*-Substituents have no detectable effect on the non-exponential factor, and with this taken as constant it was possible to calculate the contributions made by the substituents to the energy of activation from rate measurements at a single temperature. If the non-exponential factor varies, as it does when *ortho*-substituents are introduced, such contributions can be

[1] Brynmor Jones and Robinson, *J.*, 1955, 3845.
[2] Bradfield and Brynmor Jones, *J.*, 1928, 1006; Brynmor Jones, *J.*, 1935, 1831; 1942, 418, 676; Brynmor Jones and Sleight, *J.*, 1954, 1775.
[3] Stubbs and Hinshelwood, *J.*, 1949, S71.
[4] Shorter and Stubbs, *J.*, 1949, 1180.
[5] Ingold and Nathan, *J.*, 1936, 222.
[6] Evans, Gordon, and Watson, *J.*, 1937, 1430.
[7] Tommila and Hinshelwood, *J.*, 1938, 1801; Tommila, *Ann. Acad. Sci. Fennicae*, 1941, *A*, **57**, No. 13 and succeeding papers.

obtained only from the energies of activation corresponding to the substituted and unsubstituted compounds, and values thus obtained are not sufficiently accurate for examination of the validity of the additivity principle.

The effects peculiar to *ortho*-substitution are presumably steric, and therefore should be less likely to arise in the hydrolysis of esters having the ester group at some distance from the benzene ring, as in the ethyl *trans*-cinnamates, where the double bond makes the side chain rigid, and so ensures that the ester group cannot lie close to *ortho*-substituents. Furthermore, as the ethoxycarbonyl group remains conjugated with the ring, the polar effects of nuclear substituents should be qualitatively similar to those operating in the hydrolysis of benzoates, and large enough to cause rate differences measurable with sufficient accuracy.

These predictions are supported; Kindler [8] determined rates of alkaline hydrolysis for substituted ethyl cinnamates in aqueous ethanol (87·83% of ethanol w/w) and found not only that substituent effects were quite large, but also that the rates of hydrolysis of six *ortho*-substituted esters were not greatly different from those of the *para*-isomers. However, as he worked at 30° only, his data do not yield conclusions about the constancy of the non-exponential factor; nevertheless, the velocities show a marked contrast with those for the corresponding ethyl benzoates, where the fall in the non-exponential factor due to *ortho*-substitution is reflected in rate coefficients which are very much lower for *ortho*- than for the *para*-substituted esters. It is also significant that the strengths of isomeric *ortho*- and *para*-substituted cinnamic acids are of the same order, whereas the strengths of *ortho*- are very different from those of the *para*-substituted benzoic acids.[9]

Results

In order to facilitate correlation of the results with earlier ones [1, 6] for ethyl benzoates similar conditions were used. Aqueous ethanol contained 85·4% of ethanol (w/w). The velocity coefficients at 24·8° are summarised in Table 1, and Table 2 gives results for those esters whose rates of hydrolysis were measured at more than one temperature. Second-order rate constants, k, are in l. mole^{-1} sec.$^{-1}$.

Table 1. *Velocity coefficients for the alkaline hydrolysis of ethyl cinnamates at* 24·8°.

Subst.	10^3k	Subst.	10^3k	Substs.	10^3k	Substs.	10^3k
H	1·39	*p*-Pr^i	0·881	2-MeO, 3-MeO	1·15	3-NO_2, 4-MeO	3·69
o-Cl	3·48	*o*-MeO	0·517	2-Cl, 4-Cl	6·87	3-Me, 4-MeO	0·415
m-Cl	3·97	*m*-MeO	1·56	2-MeO, 4-MeO	0·189	3-MeO, 4-MeO	0·677
p-Cl	2·65	*p*-MeO	0·528	2-MeO, 5-Cl	1·54	3-MeO, 4-EtO	0·646
o-NO_2	10·1	*m*-EtO	1·51	3-Cl, 4-Cl	6·65	3-EtO, 4-EtO	0·632
m-NO_2	10·4	*p*-EtO	0·504	3-NO_2, 4-Me	6·74	3-Cl, 5-Cl	12·1
m-Me	1·16			3-NO_2, 4-Pr^i	6·69	2-MeO, 3-MeO, 4-MeO	0·526
p-Me	0·870			3-Cl, 4-MeO	1·40		

Table 2. *The non-exponential factor.*

Subst.	H	*o*-Cl	*p*-Pr^i	*p*-MeO	2-MeO, 3-MeO	3-Cl, 4-Cl	3-Cl, 4-MeO
10^3k (24·8°) ...	1·39	3·48	0·881	0·528	1·15	6·65	1·40
10^3k (35·3°) ...	3·68	9·11 †	2·38 †	1·48	3·13	17·05	3·70 †
$\log_{10} A$	10·0 *	10·0	9·9	9·9	9·9	9·9	9·8

* Derived from a linear plot of k against $1/T$ [with additional values for 10^3k at 15·05° (0·496) and 45·1° (8·83)], which also gives the energy of activation E as 17,300 cal./mole.

† Temperature, 35·1°.

Discussion

Correlations with Existing Data.—Nine esters in Table 1 were used by Kindler.[8] For these, a plot of logarithms of our velocity coefficients (k_c) against logarithms of the corresponding values from Kindler's data (k_c') shows that a linear relation $\log_{10} k_c = 1·02 \log_{10} k_c' - 0·07$ is followed sufficiently closely to indicate satisfactory agreement.

[8] Kindler, *Annalen*, 1926, **450**, 1; 1927, **452**, 90; 1928, **464**, 278; *Ber.*, 1936, **69**, 2792.

[9] Dippy, *Chem. Reviews*, 1939, **25**, 151.

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A plot of $\log_{10} k_c$ against values ($\log_{10} k_b$) for sixteen similarly-substituted ethyl benzoates [1] was also linear, individual points showing only small, random deviations from the line for the equation $\log_{10} k_c = 0{\cdot}52 \log_{10} k_b - 1{\cdot}23$. The existence of such a relation had been demonstrated.[10] It applies for substituents in the *meta*- and *para*-positions only and, if the non-exponential factors for both ester series are independent of substitution in these positions, it means that the changes in energy of activation produced by a given substitution in the two series are related by the equation $\Delta E_c = 0{\cdot}52\ \Delta E_b$. This implies that substituent effects in the cinnamic are only about half as great as in the benzoic series even though conjugation remains.

Constancy of the Non-exponential Factor.—Velocity coefficients in Tables 1 and 2 are accurate to $\pm 2\%$, and temperatures to $\pm 0{\cdot}03°$. Consequently, errors in values of $\log_{10} A$ calculated from velocity coefficients at two temperatures 10° apart are *ca.* $\pm 5\%$. That for ethyl cinnamate, based on four results ranging over 30°, is more accurate. The data in Table 2 therefore indicate that the non-exponential factor A does not vary beyond the limits of experimental error; this is true for *ortho*- as well as for *meta*- and *para*-substitutions.

Effects of Substituents on the Energy of Activation.—Increments $\Delta E'$ in the free energy of activation associated with the various substituents can be calculated from the velocity coefficients in Table 1 by means of the equation

$$\Delta E' = E' - E_0' = 2{\cdot}303\ \boldsymbol{R}T \log_{10} k/k_0$$

in which k_0 and E_0' refer to unsubstituted ethyl cinnamate, and k and E' to the substituted ester. Values of $\Delta E'$ for monosubstitution are listed in Table 3, and for polysubstitution in Table 4 ($\Delta E'_{obs.}$).

TABLE 3. *Effects of single substituents on the free energy of activation.*

	$\Delta E'$ (cal./mole)					
Subst.	Cl	NO_2	Me	Pr^i	MeO	EtO
ortho	−540	−1170	—	—	+590	—
meta	−620	−1190	+110	—	−70	−50
para	−380	—	+280	+270	+570	+600

TABLE 4. *Cumulative effects of substituents.*

Subst.	$\Delta E'_{obs.}$	$\Delta E'_{calc.}$	$10^3 k_{calc.}$	$\frac{100 k_{calc.}}{k_{obs.}}$	Subst.	$\Delta E'_{obs.}$	$\Delta E'_{calc.}$	$10^3 k_{calc.}$	$\frac{100 k_{calc.}}{k_{obs.}}$
2-MeO, 3-MeO ‡	+110	+520	0·580	50	3-NO_2, 4-*MeO* *	−580	−620	3·93	106
2-*Cl*, 4-*Cl*	−950	−920	6·63	97	3-*Me*, 4-*MeO*	+720	+680	0·441	106
2-*MeO*, 4-*MeO*	+1180	+1160	0·196	104	3-MeO, 4-MeO †	+430	+500	0·593	88
2-*MeO*, 5-*Cl*	−60	−30	1·48	96	3-MeO, 4-EtO †	+450	+530	0·566	88
3-Cl, 4-Cl †	−930	−1000	7·57	114	3-EtO, 4-EtO †	+470	+550	0·548	87
3-NO_2, 4-*Me*	−940	−910	6·47	96	3-*Cl*, 5-*Cl*	−1280	−1240	11·3	94
3-NO_2, 4-Pr^i	−930	−920	6·55	98	2-MeO, 3-MeO,	+580	+1090	0·306	58
3-*Cl*, 4-*MeO* *	0	−50	1·51	108	4-MeO ‡				

Values of $\Delta E'$ become equal to increments in the energy of activation, ΔE, if A is constant. Although this condition appears to be fulfilled, the degree of accuracy of the values of A is insufficient to justify our assuming $\Delta E' = \Delta E$. Accordingly, we first examine the cumulative effects of substituents on the free energy of activation, and then the relation between these and the corresponding effects on the energy of activation.

Cumulative Effects of Substituents.—Table 4 also contains values of $\Delta E'_{calc.}$ calculated by summation of the appropriate values from Table 3. The additivity can be judged by comparison with $\Delta E'_{obs.}$. Alternatively, observed and calculated velocity coefficients can be compared, for if the velocity coefficients for the reaction of the parent compound and two monosubstituted derivatives are, respectively, k_0, k_X, and k_Y, and if in the reaction of the corresponding disubstituted compound, velocity coefficient k_{XY}, the substituents contribute additively to the free energy of activation, then $k_{XY} = k_X k_Y / k_0$. In Table 4

[10] Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 96.

velocity coefficients thus calculated ($k_{calc.}$) are listed, and compared with the observed velocity coefficients ($k_{obs.}$) from Table 1.

The estimated limits of accuracy being taken into account, 100 $k_{calc.}/k_{obs.}$ will lie between 93 and 108 if the substituents contribute additively to the free energy of activation. Substituent effects can thus be described as additive or approximately additive in the hydrolysis of nine of the fifteen polysubstituted esters considered (those italicised in Table 4). This class includes all those in which the substituents are *meta* to each other and also, amongst several instances of 3 : 4-disubstitution, two (*) which deviated considerably from additivity of substituent effects in the alkaline hydrolysis of ethyl benzoate.

In four cases of 3 : 4-disubstitution (†) there are fairly small, but significant, deviations from additivity, and in two cases (‡) the deviations are large. A moderate deviation, in the same direction as that reported here, was found with ethyl 3 : 4-dichlorobenzoate. That the deviations recorded for 3 : 4-dialkoxy-substitution are real is apparent from their consistency: $100k_{calc.}/k_{obs.}$ for ethyl 3 : 4-dimethoxy-, 4-ethoxy-3-methoxy-, and 3 : 4-diethoxy-cinnamates, respectively, is 88, 88, and 87, and, further, 3 : 4-dimethoxy-substitution in ethyl benzoate,[1] ethyl phenylacetate,[11] and ethyl β-phenylpropionate [11] respectively it is 82, 86, and 88.

Stubbs and Hinshelwood have shown that additivity of increments in free energy of activation probably reflects a corresponding additivity in the energy of activation. We conclude that this is true for our nine cases.

The situation is less straightforward where deviations from additivity as judged on a free-energy basis are found. Such deviations might reflect deviations from additivity in the energy of activation, and/or they might be due to small (and, by our technique, undetectable) variations in A. Now, changes in A due to nuclear substitution have been measured in the alkaline hydrolysis of aromatic esters only when the substituents are close to the ester group.[6,12] In ethyl *trans*-cinnamates, however, nuclear substituents cannot be in the vicinity of the reacting group, so deviations from additivity in the free energy of activation seem less likely to result from variations in A than from deviations from additivity in the energy of activation.

Failure of substituents to contribute additively to the energy of activation may be attributed to interaction between them. Two substituents in the same molecule will polarise each other as well as the reaction centre, and this mutual interaction may modify the effect which each exerts at the reaction centre. Such polar interaction will be most pronounced when substituents capable of exerting strong conjugative effects are *ortho* or *para* to each other, and will be least with substituents *meta* to each other. Thus, it is significant that in most cases of 2 : 4- and 3 : 5-disubstitution good agreement with the concept of additivity has been found.

With substituents *ortho* to each other, steric as well as polar interactions are likely to arise. Results from 3 : 4-dialkoxy-esters suggest that there is an approximately constant interaction between the adjacent alkoxyl groups, but the data do not indicate whether this is polar or steric. The observed rates of hydrolysis may be higher than the predicted rates through the operation of a steric effect such that a 3- prevents a 4-alkoxy-group from lying in the plane of the ring, so that its electron-releasing mesomeric effect is weakened (the influence of a 3-methyl group in considerably diminishing the retarding effect of a 4-dimethylamino-group on the alkaline hydrolysis of ethyl benzoate has thus been interpreted [13]), but this is a doubtful explanation for 3 : 4-dialkoxy-substitution in view of other results in Table 4 for esters with a 4-alkoxyl group and a bulky 3-substituent (*e.g.*, methyl or nitro) which do not indicate interference with the mesomeric effect of the 4-alkoxyl group.

[11] Brynmor Jones and Watkinson, unpublished results.
[12] Fisher, Murdoch, Packer, Topsom, and Vaughan, *J.*, 1957, 4358.
[13] Price and Lincoln, *J. Amer. Chem. Soc.*, 1951, **73**, 5838.

The large discrepancies between the observed and calculated rates of hydrolysis of the 2 : 3-dimethoxy- and 2 : 3 : 4-trimethoxy-esters can be attributed with more confidence to steric interference with mesomeric electron-release from the 2-methoxy-group which is here flanked by bulky substituents in both the 1- and the 3-position. The 4-methoxy-group in ethyl 3 : 4 : 5-trimethoxybenzoate is in an analogous situation, and the results obtained [1] with this ester ($100k_{calc.}/k_{obs.} = 25$) can be similarly explained.

Experimental

Materials.—Ethyl cinnamate and nitrocinnamic acids were purchased. Other cinnamic acids were prepared from the corresponding benzaldehydes.

We thank Dr. J. Robinson for 3-chloro-4-methoxybenzaldehyde.

Cinnamic acids.[14] Benzaldehydes (0·1 mole) were heated with malonic acid (0·12—0·2 mole) and piperidine (1 ml.) in pyridine (40—50 ml., b. p. 114—116° *) at 100° until 30 min. after visible evolution of carbon dioxide had ceased (*i.e.*, usually, for 1·5—2 hr.), and the solution was then boiled for 15 min., cooled, and poured into concentrated hydrochloric acid and ice. The cinnamic acid precipitated (yield, $\geqslant$ 80%) was crystallised at least twice (thrice or more if its ethyl ester was liquid) from ethanol, slightly aqueous acetic acid, or, occasionally, benzene.

Ethyl cinnamates. Cinnamic acids (0·1 mole) were boiled with absolute ethanol (1 mole) containing 3—5% of concentrated sulphuric acid for 5 hr. and the esters were isolated by treatment of the cooled reaction mixture with saturated aqueous sodium hydrogen carbonate.

Table 5. *Cinnamic acids and ethyl cinnamates.*

	Acid	Ethyl ester				Acid	Ethyl ester	
Subst.	M. p.	M. p.	B. p.°/mm.	n_D/°c	Subst.	M. p.	M. p.	B. p.°/mm.
H	—	—	138/14	1·5592/20·5	2 : 4-Cl_2	233·5	53·5	162/5 *
o-Cl	208°	—	159/14	1·5670/20·3	3 : 4-Cl_2	218	56	156/2 [d]
m-Cl	162·5	31°	132/2	—	3 : 5-Cl_2	173·5	74	178/12
p-Cl	247·5	16	160/11	1·5768/20·4	4-Me-3-NO_2	174	95·5	191/12
o-NO_2	242·5	42	166/4	—	3-NO_2, 4-Pr^i	138	58	189/2
m-NO_2	—	75	193/10	—	5-Cl, 2-MeO	200	37·5	166/4
p-NO_2	288	137	—	—	3-Cl, 4-MeO	244 [f]	61	170/4 [g]
m-Me	118	—	146/10 *	1·5562/20·4	4-MeO, 3-NO_2	248	100	230/8
p-Me	197	—	151/4	—	4-MeO, 3-Me	201 [h]	36·5	184/11
p-Pr^i	158	—	169/14	1·5509/20·5	2 : 3-$(MeO)_2$	180	44	166/5
o-MeO	183·5	35	162/9	—	2 : 4-$(MeO)_2$	187·5	60	208/11
m-MeO	117·5	—	170/10	1·5646/20·3	3 : 4-$(MeO)_2$	180	55·5	161/2
p-MeO	171·5, 187·5 *	50	156/4	—	4-EtO, 3-MeO	200 (dec.)	109·5	—
					3 : 4-$(EtO)_2$	159·5	59	—
m-EtO	131·5	—	175/11	—	2 : 3 : 4-$(MeO)_3$	170·5	50	207/14 [k]
p-EtO	192·5, 196 *	38·5	154/2	—				

* Clearing point of mesomorphic acid.

New compounds.—[a] Found: C, 76·1; H, 7·6. $C_{12}H_{14}O_3$ requires C, 75·8; H, 7·4. [b] Found: C, 69·9; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8. [c] Found: C, 54·1; H, 4·2; Cl, 28·9. $C_{11}H_{10}O_2Cl_2$ requires C, 53·9; H, 4·1; Cl, 28·9. [d] Found: C, 53·9; H, 4·2; Cl, 29·0. [e] Found: C, 53·9; H, 4·0; Cl, 28·7. [f] Found C, 56·2; H, 4·0; Cl, 17·3. $C_{10}H_9O_2Cl$ requires C, 56·5; H, 4·3; Cl, 16·7. [g] Found: C, 60·0; H, 5·5; Cl, 14·7. $C_{12}H_{13}O_3Cl$ requires C, 59·9; H, 5·4; Cl, 14·7. [h] Found: C, 68·4; H, 6·3. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3. [i] Found: C, 71·2; H, 7·5. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3. [j] Found: C, 67·2; H, 7·4. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·3. [k] Found: C, 63·1; H, 6·8. $C_{14}H_{18}O_6$ requires C, 63·1; H, 6·8%.

Liquid esters were fractionated repeatedly under reduced pressure: solid esters were crystallised to constant m. p. from ethanol, light petroleum (b. p. of various ranges), or light petroleum–benzene, usually after being first distilled under reduced pressure. Yields were almost quantitative except from 2 : 4-dimethoxycinnamic acid. This gave mainly a substance which was apparently polymeric (a viscous liquid which slowly solidified, and was insoluble in

* This was the main fraction obtained when " redistilled " pyridine was dried over sodium hydroxide and distilled. A sample obtained in the same way from " technical " pyridine gave products which were coloured, and comparatively difficult to purify.

[14] Johnson, *Org. Reactions*, Vol. I, p. 249.

ether, soluble in acetone, and decomposed on attempted vacuum-distillation). Esterification at room temperature with hydrogen chloride as catalyst again gave mainly the polymer. A 40—50% yield of the ester was obtained when the acid was boiled for 2·5 hr. with ethanol containing 5% of toluene-*p*-sulphonic acid.

Physical date and analyses of new compounds are in Table 5.

Solvent.—" Absolute " ethanol was purified by Smith's method [15] and diluted with freshly boiled distilled water to give a mixture containing 85·4% (w/w) of ethanol (determined by specific gravity).

Velocity Measurements.—The method used was essentially that described by Evans, Gordon, and Watson.[6] Atmospheric carbon dioxide was excluded from sodium hydroxide solutions, and all solutions were standardised before or during each run. The initial concentrations of alkali and ester were equal (*ca.* 0·05M) and velocity coefficients were calculated from $k = x/at(a - x)$. All kinetics were strictly of the second order. The following details of a run with 0·0500M-ethyl *m*-methylcinnamate and 0·0500M-alkali at 24·8° are typical, zero and infinity titres being calculated from concentrations. The mean value of 10^3k is 1·16 l. mole^{-1} sec.$^{-1}$:

t (min.)	0	90	150	190	230	270	310	350	390	430	∞
Titre (ml.) ...	3·02	5·33	6·33	6·88	7·31	7·67	8·00	8·32	8·54	8·80	9·62
10^3k	—	1·17	1·16	1·17	1·17	1·15	1·15	1·17	1·15	1·17	—

Duplicate runs were carried out for all esters at 24·8° at different times (often the ester was redistilled or recrystallised between runs) and gave mean velocity coefficients agreeing to within ±1%.

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[15] Smith, quoted by Vogel, " A Textbook of Practical Organic Chemistry," Longmans, Green & Co., London, 2nd edn., 1951, p. 166.

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818. *The Condensation of* 4 : 5-*Diaminopyrimidines and Sugar Lactones.*

By R. HULL.

The product obtained from 4 : 5-diamino-6-diethylamino-2-methylpyrimidine and δ-D-gluconolactone is shown to be an 8-polyhydroxyalkylpurine by metaperiodate oxidation to the 8-formylpurine. The structure of this aldehyde has been confirmed by synthesis from the 8-hydroxymethylpurine. Some other pyrimidines appear to give similar products from either gluconoor ribono-lactones. Under similar conditions these lactones and 4 : 5 : 6-triamino-2-methylthiopyrimidine give the 5-acylaminopyrimidines.

ALTHOUGH aldonic lactones have been condensed with *o*-phenylenediamines,[1] no work appears to have been described for 4 : 5-diaminopyrimidines. Ishidate and Yuki [2] reported that condensation of some 4 : 5-diamino-pyrimidines with gluconic acid yielded the 5-acylamino-derivatives but cyclisation to the purine ring was not successful. Various workers [3] have described the preparation of polyhydroxypteridines by the condensation of aldoses, ketoses, and osones with diaminopyrimidines. Reaction of δ-D-gluconolactone and some 4 : 5-diaminopyrimidines has now been shown to yield derivatives of 8-substituted purines.

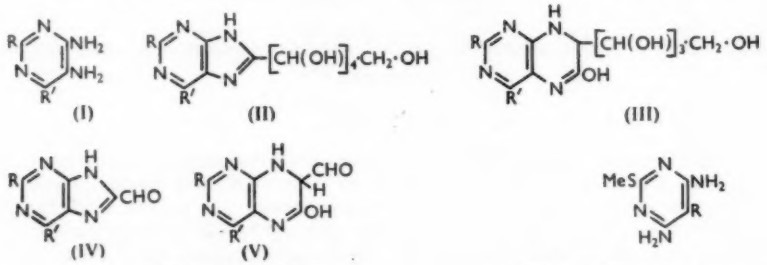
[1] Richtmyer, *Adv. Carbohydrate Chem.*, 1951, **6**, 175.
[2] Ishidate and Yuki, *Pharm. Bull.* (*Japan*), 1957, **5**, 240, 244.
[3] *E.g.*, Karrer, Schwyzer, Erden, and Siegwart, *Helv. Chim. Acta*, 1947, **30**, 1031; Petering and Weisblat, *J. Amer. Chem. Soc.*, 1947, **69**, 2566; Forrest and Walker, *J.*, 1949, 79.

XUM

8-D-Gluconolactone and 4 : 5-diamino-6-diethylamino-2-methylpyrimidine (I; R = Me, R′ = NEt_2) were fused together and yielded a compound $C_{15}H_{25}O_5N_5$ which on reaction with 4·4 mols. of metaperiodate, liberated 2·93 mols. of formic acid and gave an aldehyde $C_{11}H_{15}ON_5$. This result disproved formula (III; R = Me, R′ = NEt_2) which would have required 3 mols. of metaperiodate with the liberation of 2 mols. of formic acid to produce the dihydropteridine (V; R = Me, R′ = NEt_2); our result appears more consistent with formula (II; R = Me, R′ = NEt_2). The degradation product may be compared with Albert and Brown's 6-formyl-4 : 7-dihydroxypteridine[4] in that it did not reduce Fehling's solution. It resisted oxidation with alkaline peroxide, silver oxide, nitrogen peroxide, or nitric acid, and did not undergo a Cannizzaro reaction with alkali; however, treatment with 2 : 4-dinitrophenylhydrazine, (methylthio)thiocarbonylhydrazine,[5] and hydroxylamine yielded the expected condensation products. The oxime (VI) on treatment with acetic anhydride yielded the acetyl derivative (VII) which when heated above its m. p. readily evolved acetic acid and gave the nitrile (VIII).

A method similar to that used by Albert [6] for the synthesis of 8-hydroxymethylpurine, namely, interaction of 4 : 5-diaminopyrimidine with ethyl glycollate, was adapted to the synthesis of the alcohol (IX). Structure (IX) was proved to be correct since reduction with hydriodic acid in the presence of red phosphorus [7] yielded the 8-methylpurine (X), itself prepared in an unambiguous manner by fusion of the diaminopyrimidine (I; R = Me, R′ = NEt_2) with acetamidine hydrochloride. Oxidation of the hydroxymethyl group of (IX) with potassium dichromate gave a product identical with the metaperiodate fission product of (II; R = Me, R′ = NEt_2). These reactions thus established unequivocally formula (IV; R = Me, R′ = NEt_2) and therefore formula (II; R = Me, R′ = NEt_2) as the product of interaction of the diaminopyrimidine and gluconolactone.

In a similar fashion the morpholinopyrimidine (I; R = Me, R′ = morpholino) and gluconolactone yielded compound (II; R = Me, R′ = morpholino) which required 4·3 mols. of metaperiodate (theor., 4 mols.) to undergo degradation to 2·6 mols. of formic acid (theor., 3 mols.) and the 8-formylpurine (IV; R = Me, R′ = morpholino).



(I) (II) (III) (IV) (V)

(VI) R = CH:N·OH
(VII) R = CH:N·OAc
(VIII) R = CN
(IX) R = CH_2·OH
(X) R = Me
(XI) R = [CH(OH)]$_3$·CH_2·OH

(XII) R = NH_2
(XIII) R = NH·CO·[CH(OH)]$_n$·CH_2·OH

The same procedure applied to the pyrimidine (I; R = H, R′ = NEt_2) yielded a product in agreement with formula (II; R = H, R′ = NEt_2). Fusion of the pyrimidine (I; R = Me, R′ = NEt_2) with D-ribonolactone gave a product for which we propose formula (XI).

Finally it was found that fusion of 4 : 5 : 6-triamino-2-methylthio-pyrimidine (XII) with gluconolactone gave a product $C_{11}H_{19}O_6N_5S$ which did not appear to lose a mol.

[4] Albert and Brown, *J.*, 1953, 74.
[5] Busch, *J. prakt. Chem.*, 1916, **93**, 60.
[6] Albert, *J.*, 1955, 2690.
[7] Johnson and Chernoff, *J. Amer. Chem. Soc.*, 1914, **36**, 1742.

of water on long drying *in vacuo*. Similarly this pyrimidine (XII) with ribonolactone gave a product $C_{10}H_{17}O_5N_5S$. It was probable that in these cases only the 5-amino-group had reacted to yield the amides (XIII; $n = 4$ and 3, respectively).

The diaminopyrimidines used as starting materials were obtained by reaction of the 4-chloro-5-nitropyrimidine with the appropriate base followed by catalytic reduction of the nitro-group.

Experimental

4-Amino-6-diethylamino-2-methyl-5-nitropyrimidine.—Diethylamine (12·5 ml.) was added dropwise to a cooled stirred solution of 4-amino-6-chloro-2-methyl-5-nitropyrimidine [8] (7·56 g.) in ethyl acetate (280 ml.) and set aside for 2 days. The solvent was removed under diminished pressure and the residue (9·0 g.) was collected and washed with water. Recrystallisation from aqueous alcohol gave the *diethylaminopyrimidine* as pale yellow prismatic needles, m.p. 109·5—110·5° (Found: C, 48·15; H, 7·1; N, 30·9. $C_9H_{15}O_2N_5$ requires C, 48·0; H, 6·6; N, 31·1%).

4 : 5-Diamino-6-diethylamino-2-methylpyrimidine.—4-Amino-6-diethylamino-2-methyl-5-nitropyrimidine (8·7 g.) was reduced with hydrogen at laboratory temperature and pressure in the presence of Raney nickel. After filtration and evaporation the *diaminopyrimidine* (7·6 g.) crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 117—118° (Found: C, 55·85; H, 9·0; N, 35·5. $C_9H_{17}N_5$ requires C, 55·4; 8·7; N, 35·9%).

*6-Diethylamino-8-*D*-gluco**pentahydroxypentyl**-2-methylpurine.*—4 : 5-Diamino-6-diethylamino-2-methylpyrimidine (1·95 g.) and δ-D-gluconolactone (1·96 g.) were heated in a bath at 140—150° for 10 min. Extraction of the cooled mixture with water (charcoal) gave the *purine* (1·2 g.) which recrystallised from water in needles, m. p. 229°, $[\alpha]_D^{21} + 41°$ (*c* 3·33 in 0·1N-hydrochloric acid) (Found: C, 50·1; H, 6·4; N, 19·6. $C_{15}H_{25}O_5N_5$ requires C, 50·7; H, 7·0; N, 19·7%).

4-Amino-2-methyl-6-morpholino-5-nitropyrimidine.—Morpholine (7·6 g.) was added slowly to a stirred solution of 4-amino-6-chloro-2-methyl-5-nitropyrimidine [8] (7·6 g.) in ethyl acetate (280 ml.), then kept for 2 days. The morpholine hydrochloride was collected and washed with ethyl acetate, and the filtrates were evaporated to dryness. The *morpholinopyrimidine* (9·0 g.) recrystallised from aqueous alcohol in pale yellow prismatic needles, m. p. 193·5—195° (Found: C, 45·3; H, 5·5; N, 29·25. $C_9H_{13}O_3N_5$ requires C, 45·2; H, 5·45; N, 29·3%).

4 : 5-Diamino-2-methyl-6-morpholinopyrimidine.—4-Amino-2-methyl-6-morpholino-5-nitropyrimidine (2·25 g.), suspended in methanol (150 ml.), was reduced with hydrogen at laboratory temperature and atmospheric pressure in presence of Raney nickel. After filtration and evaporation the residue (2 g.) recrystallised from ethyl acetate to give the *diaminopyrimidine* as plates, m. p. 191° (Found: C, 52·0; H, 7·0; N, 33·95. $C_9H_{15}ON_5$ requires C, 51·7; H, 7·2; N, 33·5%).

*2-Methyl-6-morpholino-8-*D*-gluco**pentahydroxypentyl**purine.*—A ground mixture of 4 : 5-diamino-2-methyl-6-morpholinopyrimidine (1·05 g.) and δ-D-gluconolactone (0·98 g.) was heated in a bath at 140° until a complete melt was obtained, then for 10 min. during which the melt began to solidify. Extraction of the mixture with boiling water (charcoal) gave the *purine* as pale yellow needles, m. p. 260°, $[\alpha]_D^{21} + 39°$ (*c* 3·093 in 0·1N-hydrochloric acid) (Found: C, 48·65; H, 6·2; N, 18·75. $C_{15}H_{23}O_6N_5$ requires C, 48·8; H, 6·25; N, 18·95%).

Fission of Hydroxyalkylpurines with Sodium Metaperiodate.—The hydroxyalkylpurine (*ca.* 0·4 millimole) was dissolved in hot water, quickly cooled, treated with 0·2039M-sodium metaperiodate (10 ml.) and set aside for 24 hr. The solution was diluted to a known volume, an aliquot part was removed, and the unchanged metaperiodate estimated iodometrically by Barneby's method [9] using 0·1N-sodium arsenite. Formic acid was estimated in an aliquot part by titration with 0·1N-sodium hydroxide (Methyl Red).

Isolation of 6-Diethylamino-8-formyl-2-methylpurine.—Neutralisation of the acid reaction mixture of 6-diethylamino-2-methyl-8-D-*gluco*pentahydroxypentylpurine and sodium metaperiodate gave a solid which was collected and washed with water. Recrystallisation from aqueous alcohol gave the *aldehyde* as colourless needles, m. p. 210·5—211° (Found: C, 56·95; H, 6·2; N, 29·9. $C_{11}H_{15}ON_5$ requires C, 56·7; H, 6·45; N, 30·0%). It does not reduce Fehling's solution, but blackens warm ammoniacal silver nitrate solution.

Isolation of 8-Formyl-2-methyl-6-morpholinopurine.—In a similar manner neutralisation of

[8] Boon, Jones, and Ramage, *J.*, 1951, 96.
[9] Barneby, *J. Amer. Chem. Soc.*, 1916, **38**, 330.

the reaction mixture from 2-methyl-6-morpholino-8-D-*gluco*pentahydroxypentylpurine and sodium metaperiodate and subsequent treatment with sodium hydrogen carbonate gave the *aldehyde* which crystallised from butanol in needles, m. p. 285° (decomp.) (Found: C, 54·15; H, 5·45; N, 27·8. $C_{11}H_{13}O_2N_5$ requires C, 53·45; H, 5·3; N, 28·3%).

Compounds from 6-*Diethylamino*-8-*formyl*-2-*methylpurine*.—The 2 : 4-*dinitrophenylhydrazone hydrochloride* crystallised from butanol as yellow needles, m. p. 294° (decomp.) (Found: C, 44·05; H, 4·85. $C_{17}H_{19}O_4N_9,HCl,H_2O$ requires C, 43·65; H, 4·7%).

The condensation *product* with (methylthio)thiocarbonylhydrazine [5] crystallised from butanol as yellow needles, m. p. 234° (decomp.) (Found: C, 46·6; H, 6·1; N, 28·7. $C_{13}H_{19}N_7S_2$ requires C, 46·3; H, 5·6; N, 29·1%).

The aldehyde (3·8 g.) in hot alcohol (120 ml.) was added to a solution of hydroxylamine [prepared by adding a solution of hydroxylamine hydrochloride (1·42 g.) in water (2 ml.) to a solution from sodium (0·47 g.) in alcohol (12 ml.) and filtering], and the whole was heated under reflux during 30 min. The *oxime* (3·8 g.) was collected from the cooled mixture. It crystallised from alcohol as needles, m. p. 238° (decomp.) (Found: C, 53·6; H, 6·8; N, 34·1. $C_{11}H_{16}ON_6$ requires C, 53·25; H, 6·45; N, 33·9%).

8-*Cyano*-6-*diethylamino*-2-*methylpurine*.—6-Diethylamino-2-methylpurine-8-aldoxime (2·75 g.) and acetic anhydride (25 ml.) were heated under reflux for 15 min. Excess of reagent was removed under diminished pressure. Recrystallisation of the residue from alcohol gave the *acetyl derivative* of the oxime (1·8 g.) as pale yellow needles, m. p. 189° (decomp.), resolidifying, and remelting at 299° (Found: C, 54·5; H, 6·1; N, 30·9. $C_{13}H_{18}O_2N_6$ requires C, 53·8; H, 6·2; N, 29·0%). The above acetyl compound (1·2 g.) was heated to 190°, acetic acid being liberated. Aqueous sodium hydrogen carbonate was added to the cooled residue and the solid (0·95 g.) was collected and washed with water. Recrystallisation from 2-ethoxyethanol gave the *cyanopurine* as needles, m. p. 302° (Found: C, 57·3; H, 6·2; N, 36·2. $C_{11}H_{14}N_6$ requires C, 57·4; H, 6·1; N, 36·5%).

6-*Diethylamino*-8-*hydroxymethyl*-2-*methylpurine*.—4 : 5-Diamino-6-diethylamino-2-methylpyrimidine (1·0 g.) and ethyl glycollate (2·15 g.) were heated together in an open flask in a bath at 140° during 2 hr. Ether was added to the cooled mixture, and the solid (0·9 g.) was collected and washed with ether. Two recrystallisations from toluene (charcoal) gave the *hydroxymethylpurine* as needles, m. p. 210° (Found: C, 55·7; H, 7·0; N, 29·2. $C_{11}H_{17}ON_5$ requires C, 56·15; H, 7·25; N, 29·8%).

6-*Diethylamino*-2 : 8-*dimethylpurine*.—A mixture of 4 : 5-diamino-6-diethylamino-2-methylpyrimidine (0·72 g.) and acetamidine hydrochloride (0·38 g.) was heated in a bath at 160° during 20 min. A slight excess of aqueous sodium hydrogen carbonate was added to the cooled melt and later the solid was collected. Recrystallisation from light petroleum (b. p. 100—120°) gave the *dimethylpurine* as needles, m. p. 166° (Found: C, 60·5; H, 7·5; N, 32·0. $C_{11}H_{17}N_5$ requires C, 60·3; H, 7·7; N, 32·0%).

Oxidation of 6-*Diethylamino*-8-*hydroxymethyl*-2-*methylpurine*.—Finely powdered potassium dichromate (0·25 g.) was added slowly to a stirred solution of 6-diethylamino-8-hydroxymethyl-2-methylpurine (0·5 g.) in acetic acid (10 ml.) in a bath at 80°. After a further 1 hr. the mixture was cooled and neutralised with sodium hydrogen carbonate, and the product (0·3 g.) was collected and washed with water. Recrystallisation from aqueous alcohol gave the 8-formyl-purine, m. p. 213°. A mixed m. p. with the periodate oxidation product (m. p. 211°) was 210°. The infrared spectrum (in Nujol) contains a band at 1700 cm.$^{-1}$ (CO); the band at 3210 cm.$^{-1}$ (OH), present in the starting material, had disappeared. The condensation product with (methylthio)-thiocarbonylhydrazine had m. p. 231° (decomp.).

Reduction of 6-*Diethylamino*-8-*hydroxymethyl*-2-*methylpurine*.—Red phosphorus (0·05 g.) was added to a solution of 8-hydroxymethyl-6-diethylamino-2-methylpurine (0·25 g.) in hydriodic acid (*d* 1·7; 4·5 ml.), and the whole was heated under reflux during 3 hr. The cooled mixture was filtered and the filtrates were neutralised with aqueous sodium hydrogen carbonate. The solid (0·14 g.; m. p. 161°) was collected and washed with water. Recrystallisation from light petroleum (b. p. 100—120°) gave 6-diethylamino-2 : 8-dimethylpurine, m. p. 165—166°. It was undepressed in admixture with and had a similar infrared absorption spectrum to an authentic sample.

6-*Diethylamino*-8-D-gluco*pentahydroxypentylpurine*.—4 : 5-Diamino-6-diethylaminopyrimidine [10] (1·0 g.) and δ-D-gluconolactone (0·99 g.) were heated in a bath at 120° during 2½ hr.

[10] Boon and Jones, *J.*, 1951, 591.

Two recrystallisations from a small quantity of water gave the *purine* as needles, m. p. 188—189·5° (Found: C, 48·7; H, 7·1; N, 20·35. $C_{14}H_{23}O_5N_5$ requires C, 49·25; H, 6·75; N, 20·5%).

*6-Diethylamino-2-methyl-8-*D*-ribotetrahydroxybutylpurine.*—4 : 5-Diamino-6-diethylamino-2-methylpyrimidine (1·95 g.) and D-ribonolactone (1·62 g.) were heated in a bath at 140° ± 5° during 10 min. The cooled mixture was extracted with a small quantity of hot water. Crystallisation of the residue from butanol gave the *purine* as needles, m. p. 228—229° (sintering at 220°), $[\alpha]_D^{24}$ − 20° (*c* 3·098 in pyridine) (Found: C, 51·85; H, 7·25; N, 21·5 $C_{14}H_{23}O_4N_5$ requires C, 51·7; H, 7·1; N, 21·6%).

*Reaction of 8-*D*-Gluconolactone with 4 : 5 : 6-Triamino-2-methylthiopyrimidine.*—8-D-Gluconolactone (1·04 g.) and 4 : 5 : 6-triamino-2-methylthiopyrimidine [11] (1·0 g.) were heated to fusion in a bath at 140° during 30 min. Extraction of the cooled melt with boiling water (charcoal) gave the *product* (0·97 g.) as prisms, m. p. 184—185°, $[\alpha]_D^{22}$ + 58° (*c*, 2·991 in 5% citric acid) (Found: C, 37·95; H, 5·65; N, 19·9. $C_{11}H_{19}O_6N_5S$ requires C, 37·83; H, 5·45; N, 20·0%). The compound did not appear to lose water on long drying *in vacuo*, and was probably 4 : 6-diamino-5-D-gluconamido-2-methylthiopyrimidine.

Reaction of D-Ribonolactone with 4 : 5 : 6-Triamino-2-methylthiopyrimidine.—A mixture of D-ribonolactone (1·56 g.) and 4 : 5 : 6-triamino-2-methylthiopyrimidine (1·71 g.) was heated to a fused mass in a bath at 140° during 15 min. Repeated crystallisation of the cooled mixture from water gave a *product* as colourless needles, m. p. 224—225°, $[\alpha]_D^{21}$ + 28° (*c* 4·029 in 5% citric acid) (Found: C, 35·05; H, 5·6; N, 21·3. $C_{10}H_{17}O_5N_5S,H_2O$ requires C, 35·6; H, 5·6; N, 20·75%). The compound was probably the monohydrate of 4 : 6-diamino-2-methylthio-5-D-ribonamidopyrimidine.

The author thanks Mr. K. Thompson and Dr. J. M. Pryce for the infrared absorption determinations.

IMPERIAL CHEMICAL INDUSTRIES LIMITED,
PHARMACEUTICALS DIVISION, ALDERLEY PARK,
MACCLESFIELD, CHESHIRE.

[*Received, June 11th*, 1958.]

[11] Baddiley, Lythgoe, McNeil, and Todd, *J.*, 1943, 385.

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819. *Polycyclic Cinnoline Derivatives. Part I. Reduction of 2 : 2′-Dinitrodiaryls and Related Compounds.*

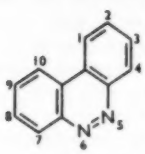
By R. S. W. BRAITHWAITE, P. F. HOLT, and A. N. HUGHES.

Methods for the reduction of 2 : 2′-dinitrodiaryls, 5 : 6-dinitroacenaphthene, and 1 : 8-dinitronaphthalene have been studied, to facilitate the preparation of polycyclic cinnoline derivatives. Direct reduction may give a polycyclic cinnoline derivative, its *N*-oxide, an amine, a nitroamine, or a polymer.

CERTAIN polycylic cinnoline derivatives would be interesting as analogues of carcinogens, but few complex cinnoline derivatives are known, and there has been little study of the general preparative methods. The formation of a ring-homologous cinnoline system usually involves synthesis and reduction of a 2 : 2′-dinitrodiaryl but the yields are sometimes poor. The reduction of 6 : 6′-dinitrobenzidine, 6 : 6′-dinitro-*o*-tolidine, 4 : 4′-dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls (halogen = Cl, Br, and I) and 2 : 6 : 2′ : 6′-tetranitrodiphenyl has now been examined, and also that of 5 : 6-dinitroacenaphthene (Ring Index numbering, No. 1779) and 1 : 8-dinitronaphthalene where an internal azo-link can be formed. The reducing agents used were lithium aluminium hydride, zinc in aqueous-alcoholic potassium hydroxide, sodium amalgam in methanol or ethanol, aqueous-alcoholic sodium sulphide, and aqueous-alcoholic sodium polysulphide. From published results [1] it would seem that from simple 2 : 2′-dinitrodiaryls aqueous-ethanolic sodium

[1] Simpson, "Condensed Pyridazine and Pyrazine Rings," Interscience Publ., New York, 1953, p. 53.

sulphide normally forms an *N*-oxide, electrolytic reduction a cinnoline, sodium amalgam in methanol a cinnoline, and zinc dust in potassium hydroxide the mono- and the di-*N*-oxide. We find that the reduction products may also include amines and polymers, and that nuclear halogen may be eliminated.



(I)

Lithium Aluminium Hydride.—Benzo[*c*]cinnoline (I) has been prepared [2,3] (90% yield) by reducing 2 : 2′-dinitrodiphenyl with lithium aluminium hydride. This reducing agent normally gave satisfactory yields (70—90%) of cinnoline when applied to the sterically unhindered dinitro-compounds listed above, but the nitroamines were not reduced unless a large excess of the reagent was used because an initial reaction involving the amino-groups utilises 0·5 mol. of the reagent.

Mićović and Mihailović [4] quote a number of authors as stating that nuclear halogen is not eliminated under normal conditions during reductions with lithium aluminium hydride. In the production of cinnolines we find that chlorine and bromine are unaffected, but that iodine is eliminated, from 4 : 4′-dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls. (Hill [2] found that the reduction of *o*-chloronitrobenzene gives azobenzene.) 2 : 6 : 2′ : 6′-Tetranitrodiphenyl gives a polymer and not a cinnoline.

Zinc and Potassium Hydroxide.—Täuber,[5] using a slight excess of zinc dust and potassium hydroxide in aqueous ethanol to reduce 2 : 2′-dinitrodiphenyl, obtained a mixture of benzo[*c*]cinnoline mono- and (mostly) di-*N*-oxide. 4 : 4′-Dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls (halogen = Cl, Br, or I) all gave cinnolines, but bromine and iodine were removed.

Sodium Sulphide.—Sodium sulphide and aqueous ethanol, first used to form cinnoline derivatives by Ullmann and Dieterle,[6] have usually given *N*-oxides. We confirmed this. The retention or elimination of nuclear-substituted iodine can depend on the alkalinity of the reducing agent. When sodium sulphide and sodium hydroxide are used 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gives the cinnoline oxide containing only one atom of iodine, but sodium sulphide alone gives the di-iodocinnoline oxide.

Certain dinitro-compounds do not give the expected cyclic azo-compounds. 1 : 8-Dinitronaphthalene gives a polymer with aqueous-ethanolic sodium sulphide although under some other reducing conditions it gives an intramolecular hydrazo-compound.[7] Likewise, 2 : 6 : 2′ : 6′-tetranitrodiphenyl and 5 : 6-dinitroacenaphthene give polymers. In the latter case even aqueous-ethanolic sodium hydroxide produces a polymer, though this reagent does not reduce the dinitronaphthalene. When polymers are formed, the yield is approximately constant over a wide range of experimental conditions, indicating that the polymer is not an intermediate in the production of other soluble end-products, such as amines.

Sodium Polysulphide.—This reagent reduced 2 : 6 : 2′ : 6′-tetranitrodiphenyl to 2-amino-6 : 2′ : 6′-trinitrodiphenyl and a diaminodinitrodiphenyl. The latter could be 2 : 6-diamino-2′ : 6′-dinitrodiphenyl but is most probably 2 : 2′-diamino-6 : 6′-dinitrodiphenyl since, by analogy with the reduction of 1 : 3-dinitrobenzene with sodium polysulphide (when one nitro-group only is reduced), it is improbable that both nitro-groups in one ring of the diphenyl molecule would be reduced.

Sodium Amalgam and Alcohol.—Sodium amalgam and methanol has been reported generally to give a cinnoline (Täuber [5] and, later, others). Our results confirm that cinnolines are normally formed although 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gives a mixture of the cinnoline and its oxide. Nuclear chlorine and bromine are

[2] Hill, Ph.D. thesis, University of Reading, 1952.
[3] Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[4] Mićović and Mihailović, "Lithium Aluminium Hydride in Organic Chemistry," Serbian Academy of Sciences, Belgrade, 1955, p. 104.
[5] Täuber, *Ber.*, 1891, **5**, 3081.
[6] Ullmann and Dieterle, *Ber.*, 1904, **37**, 23.
[7] Vorozhtsov and Kozlov, *J. Gen. Chem. U.S.S.R.*, 1937, **7**, 793.

unaffected but iodine is eliminated when 4 : 4′-dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls are reduced. 2 : 6 : 2′ : 6′-Tetranitrodiphenyl and the diaminodinitrodiphenyl obtained above are reduced to 2 : 6 : 2′ : 6′-tetra-aminodiphenyl. Different products may be obtained if ethanol rather than methanol is used in the reduction. Thus 2 : 6 : 2′ : 6′-tetranitrodiphenyl yields a polymer with sodium amalgam and ethanol, but the tetramine with sodium amalgam and methanol.

The results fit the generalisation that 2 : 2′-dinitrodiphenyls give cinnolines with lithium aluminium hydride and with sodium amalgam, but *N*-oxides with sodium sulphide. 2 : 6 : 2′ : 6′-Tetranitro- and 2 : 2′-diamino-6 : 6′-dinitro-diphenyl are exceptions; cinnolines are not formed, possibly because of steric hindrance. Similarly, an internal azo-link is not formed from 1 : 8-dinitronaphthalene and 5 : 6-dinitroacenaphthene. In all these cases amines, nitroamines, or polymeric azo-compounds are produced. Under some conditions, methyl groups in the 6- and the 6′-position of 2 : 2′-dinitrodiphenyl permit cinnoline formation,[8,9] although nitroamines may also be formed.[9]

Bismark Brown and the reduction products of *m*-dinitrobenzene derivatives appear to be the only known polymers similar to the azo- and azoxy-polymers here described. The latter, however, appear to be of high molecular weight. Hill [2] found that *m*-dinitrobenzene is reduced by lithium aluminium hydride to a product similar to Bismark Brown, and others [10] produced substances which were probably not simple reduction products from substituted *m*-dinitrobenzenes.

The polymeric azo- and azoxy-compounds reported here are black, hygroscopic, infusible, and insoluble in all the common solvents. Some are slightly soluble in dimethylformamide to give intensely coloured solutions. Probably owing to their refractory nature and to their avidity for moisture, widely varying values were obtained in replicate analyses. The values, always very low, were somewhat increased if a higher temperature of combustion was used. Evidently the Liebig and the Dumas methods are inadequate.

Experimental

Preparation of oo′*-Dinitro-compounds.*—*4 : 4′-Dichloro-, 4 : 4′-dibromo-, and 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl.* 6 : 6′-Dinitro-*o*-tolidine [11] (10 g.) was tetrazotised with sodium nitrite (20 g.) in concentrated sulphuric acid (140 ml.) at 0°, diluted with acetic acid (120 ml.), and poured into cuprous chloride (10 g.) in concentrated hydrochloric acid (300 ml.), cuprous bromide (10 g.) in 60% hydrobromic acid (300 ml.), or potassium iodide (50 g.) in water (100 ml.). (Iodine was removed with sodium hydroxide and thiosulphate.) The precipitate in acetone solution was boiled with charcoal. The filtered solution gave yellow needles of the dichloro- (9·3 g.), dibromo- (9·9 g.), or di-iodo-compound (9·3 g.).

Recrystallisation gave 4 : 4′-dichloro- (from aqueous acetone), m. p. 217° (lit.,[12] m. p. 211—212°), 4 : 4′-dibromo- (from aqueous acetone), m. p. 240° (lit.,[12] m. p. 230—233°), and 4 : 4′-*di-iodo*-3 : 3′-*dimethyl*-6 : 6′-*dinitrodiphenyl* (from benzene), yellow needles, m. p. 230—233° (Found: C, 32·5; H, 2·2; N, 5·3; I, 48·7. $C_{14}H_{10}O_4N_2I_2$ requires C, 32·2; H, 1·9; N, 5·3; I, 48·5%). These compounds slowly decompose under the influence of light.

Reduction of Dinitro-compounds.—(a) *With lithium aluminium hydride.* The dinitro-compound (1 g.) in benzene–ether was refluxed with an excess of lithium aluminium hydride in ether. The excess of hydride was decomposed by the addition of water, the resulting mixture filtered, and the filtrate concentrated. A solid product was separated by filtration and was recrystallised from benzene. By this method 6 : 6′-dinitro-*o*-tolidine gave 3 : 8-diamino-2 : 9-dimethylbenzo[*c*]cinnoline (0·15 g.), m. p. 272—274° (decomp.); 6 : 6′-dinitrobenzidine gave 3 : 8-diaminobenzo[*c*]cinnoline (0·13 g.), m. p. 265°; 4 : 4′-dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-*dichloro*-2 : 9-*dimethylbenzo*[c]*cinnoline* (0·6 g.), yellow bars, m. p. 279° (Found: C, 60·0;

[8] Wittig and Stichnoth, *Ber.*, 1935, **68**, 928.
[9] Sako, *Bull. Chem. Soc. Japan*, 1934, **9**, 393.
[10] Meyer and Michler, *Ber.*, 1873, **6**, 746; Michler, *Ber.*, 1874, **7**, 421; *Ann. Chem. Pharm.*, 1875, **175**, 152; Meier and Böhler, *Chem. Ber.*, 1956, **89**, 2301.
[11] Beilstein's "Handbuch der organischen Chemie," 4th edn., Vol. 13, p. 261.
[12] Le Fèvre and Turner, *J.*, 1928, 963.

XUM

H, 3·8; N, 10·0; Cl, 26·0. $C_{14}H_{10}N_2Cl_2$ requires C, 60·6; H, 3·6; N, 10·1; Cl, 25·7%); 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-*dibromo*-2 : 9-*dimethylbenzo*[*c*]*cinnoline* (0·69 g.) as yellow needles, m. p. 280° (Found: C, 45·7; H, 2·8; N, 7·7; Br, 43·9. $C_{14}H_{10}N_2Br_2$ requires C, 45·9; H, 2·7; N, 7·7; Br, 43·7%); and 4 : 4′-di-iodo-5 : 5′-dimethyl-2 : 2′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·18 g.), m. p. 185°. 2 : 6 : 2′ : 6′-Tetranitrodiphenyl gave a polymeric azo-compound, dissolving in sulphuric acid (*d* 1·84) to a dark brown solution from which the polymer was reprecipitated by water, and in strong aqueous sodium hydroxide to give a purple solution from which the polymer was reprecipitated by acid. No sample was completely free from ash.

(b) *With zinc and potassium hydroxide.* Aqueous 40% potassium hydroxide was added to the dinitro-compound (1 g.) in hot ethanol. An excess of zinc dust was added to the boiling solution. After 10 min. the liquid was filtered, concentrated, and diluted with water. The solid which separated was dissolved in acetone or benzene, and the solution was boiled with charcoal. After concentration, a crystalline product separated. By this method, 4 : 4′-dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dichloro-2 : 9-dimethylbenzo[*c*]cinnoline (0·6 g.), m. p. 279°; 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·16 g.), m. p. 185°; 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·26 g.), m. p. 186°.

(c) *With sodium amalgam and alcohol.* An excess of sodium amalgam was added to the di- or tetra-nitro-compound (1 g.) in dry methanol. After several hours' stirring the mixture was boiled and filtered. The filtrate was evaporated and water added.

4 : 4′-Dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dichloro-2 : 9-dimethylbenzo-[*c*]cinnoline (0·23 g.), m. p. 277°. 4 : 4′-Dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dibromo-2 : 9-dimethylbenzo[*c*]cinnoline (0·1 g.), m. p. 280°, soluble in benzene, and its 5-*oxide* (0·04 g.), m. p. 284° (decomp.) (Found: C, 44·3; H, 2·7; N, 7·2; Br, 42·0. $C_{14}H_{10}ON_2Br_2$ requires C, 44·0; H, 2·6; N, 7·3; Br, 42·0%), insoluble in benzene and recrystallised from dimethylformamide. 4 : 4′-Di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·23 g.), needles (from acetone), m. p. 184°. 2 : 6 : 2′ : 6′-Tetranitrodiphenyl gave 2 : 6 : 2′ : 6′-*tetra-aminodiphenyl* (0·26 g.), needles (from ether) or prisms (from benzene), m. p. 200° (Found: C, 67·8; H, 6·9. $C_{12}H_{14}N_4$ requires C, 67·3; H, 6·6%). 2 : 2′(?)-Diamino-6 : 6′(?)-dinitrodiphenyl (24 mg.) gave 2 : 6 : 2′ : 6′-tetra-aminodiphenyl (12 mg.), m. p. 197—198°.

2 : 6 : 2′ : 6′-Tetranitrodiphenyl was reduced by this procedure, but with ethanol replacing methanol. A black polymeric azo-compound (0·4 g.) was precipitated similar to that produced with lithium aluminium hydride.

(d) *With sodium sulphide.* Aqueous sodium sulphide was added to the polynitro-compound (1 g.), dissolved in boiling 90% ethanol, and the mixture was refluxed for ½—2 hr. Water was added and the product was filtered off and recrystallised or purified by chromatography on alumina.

By this method 4 : 4′-dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-*dichloro*-2 : 9-*dimethylbenzo*[*c*]*cinnoline* 5-*oxide* (0·3 g.), a light yellow powder (from dimethylformamide), m. p. 275° (decomp.) (Found: C, 56·6; H, 3·5; N, 9·8; Cl, 24·4. $C_{14}H_{10}ON_2Cl_2$ requires C, 57·3; H, 3·4; N, 9·6; Cl, 24·2%); 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dibromo-2 : 9-dimethylbenzo[*c*]cinnoline 5-oxide (0·27 g.), pale yellow needles (from dimethylformamide), m. p. 286° (decomp.); 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-di-iodo-2 : 9-dimethylbenzo[*c*]cinnoline 5-oxide with acetone of crystallisation (31 mg.), as yellow crystals from acetone. The material could not be freed from acetone because of its thermal instability (Found: C, 38·4; H, 2·4; I, 48·8. Calc. for $C_{14}H_{10}ON_2I_2,C_3H_6O$: C 38·2; H, 3·0; I, 47·6%). The material was unstable in light, the m. p. 242—246° (decomp.) falling to *ca.* 225° in a few hours. If the reduction was carried out with added sodium hydroxide, the product was 2 : 9-*dimethyl*-3-*iodobenzo*[*c*]*cinnoline* 5-*oxide* (37 mg.), m. p. 212—215° (decomp.) (Found: C, 48·0; H, 3·4; I, 36·2. $C_{14}H_{11}ON_2I$ requires C, 48·0; H, 3·1; I, 36·3%). Repetition of this reduction did not always give an identical product, but, probably, a mixture of mono- (mainly) and di-iodo-compounds (*e.g.*, Found: C, 42·8; I, 46·6; C, 43·2; I, 44·0; C, 41·7; I, 44·0%).

1 : 8-Dinitronaphthalene and 2 : 6 : 2′ : 6′-tetranitrodiphenyl gave impure polymeric azo-compounds.

2 : 6 : 2′ : 6′-Tetranitrodiphenyl (1 g.), boiled with sodium sulphide (1·5 g.) and sulphur

(1·5 g.) in hot ethanol, gave an amine which was extracted with ether, transferred to water as the hydrochloride, then again extracted with ether after basification. The ethereal solution yielded *2-amino-6 : 2′ : 6′-trinitrodiphenyl* (0·14 g.), m. p. 159—160°, orange prisms from ethanol (Found: C, 47·7; H, 2·9; N, 18·8. $C_{12}H_8O_6N_4$ requires C, 47·4; H, 2·6; N, 18·5%). An excess of sulphide (sodium sulphide, 10 g.; sulphur, 3 g.) gave *2 : 2′(?)-diamino-6 : 6′(?)-dinitrodiphenyl* (87 mg.), as orange blades (from ethanol), m. p. 241° (Found: C, 53·0; H, 3·6. $C_{12}H_{10}O_4N_4$ requires C, 52·6; H, 3·7%).

(e) *With sodium hydroxide in ethanol.* 5 : 6-Dinitroacenaphthene (0·65 g.) in ethanol (300 ml.) and acetone (20 ml.) was refluxed with sodium hydroxide (0·9 g.) in water (10 ml.), then acidified. A black infusible polymeric azo-compound (0·5 g.) was formed.

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UNIVERSITY OF READING. [*Received, June 17th,* 1958.]

820. *Studies in the Synthesis of Mycolic Acid.*

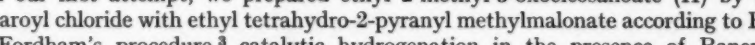
By E. D. MORGAN and N. POLGAR.

A synthetic route to mycolic acid involving conversion of an α-halogenoalkyl methyl ether, by malonic ester condensation, into an α-alkyl-substituted β-methoxy-acid has been examined. In a model experiment, 3-methoxy-2-propylpentanoic acid (VII; R = H) was prepared, and by further processes transformed into ethyl 2-(1-hydroxy-3-methoxy-2-propylpentyl)eicosanoate (X). In another series of experiments ethyl 5-chloro-2-ethoxycarbonyl-3-methoxy-2-propylpentanoate (V) was synthesised from 1 : 3-dichloropropyl methyl ether (IV) and ethyl propylmalonate, with a view to utilising the terminal chlorine for attachment of a long carbon chain.

The preparation of ethyl 3-hydroxy-2-methyleicosanoate (III) through ethyl 2-methyl-3-oxoeicosanoate (II) is also described.

THE present work was undertaken concurrently with the degradative studies of mycolic acid already described.[1] In the initial stages of this work it appeared of interest to synthesise, as models, branched-chain β-hydroxy-acids with a methoxyl group in the δ-position, and alkyl branches in the α- and γ-positions to the carboxyl group, thus having a structure corresponding to formula (I) (where R and R′ are alkyl chains) which has been proposed by Aebi, Vilkas, and Lederer [2] for an acid isolated from the strain " Brèvannes " of tubercle bacilli. Although in our earlier communication [1] we concluded that in our sample of mycolic acid the methoxyl group is farther away from the carboxyl group, the present synthetic studies were continued; the synthetic route described below could be readily modified to introduce the requisite alkyl residue between the carbon atoms bearing the hydroxyl and the methoxyl group.

In our first attempt, we prepared ethyl 2-methyl-3-oxoeicosanoate (II) by reaction of stearoyl chloride with ethyl tetrahydro-2-pyranyl methylmalonate according to Bowman and Fordham's procedure,[3] catalytic hydrogenation in the presence of Raney nickel (cf. Skogh [4]) then giving the hydroxy-ester (III). We then tried to *O*-methylate this



ester, with the intention of using the methoxy-acid chloride as starting point for processes analogous to those given above for stearoyl chloride; however, various attempts to methylate the hydroxy-ester (III) were unsuccessful.

[1] Morgan and Polgar, *J.*, 1957, 3779.
[2] Aebi, Vilkas, and Lederer, *Bull. Soc. chim. France*, 1954, 79.
[3] Bowman and Fordham, *J.*, 1952, 3945.
[4] Skogh, *Acta Chem. Scand.*, 1952, **6**, 809.

In further experiments, we studied the condensation of α-halogenoalkyl ethers with a sodiomalonic ester (cf. ref. 5), to give, after hydrolysis and decarboxylation, a β-alkoxy-acid. First, 1 : 3-dichloropropyl methyl ether (IV), readily available from acraldehyde by addition of hydrogen chloride and methanol,[6] was converted by reaction with ethyl sodio-propylmalonate into ethyl 5-chloro-2-ethoxycarbonyl-3-methoxy-2-propylpentanoate (V), and we intended to utilise the terminal chlorine for attaching a long carbon chain. Since this chain-lengthening involves known procedures, we decided to test the remaining stages of the proposed synthesis by using, meanwhile, as a model ethyl 2-ethoxycarbonyl-3-methoxy-2-propylpentanoate (VI); this was obtained by condensation of 1-chloropropyl methyl ether (cf. ref. 7) with ethyl sodiopropylmalonate. The same product (VI) resulted on reduction of the chloro-ester (V) by means of zinc amalgam and acetic acid; this confirmed the structure (V) assigned to the chloro-ester.

Difficulties were experienced with the conversion of the malonic ester (VI) by the usual successive stages (hydrolysis, decarboxylation) into the β-methoxy-acid (VII; R = H) owing to partial loss of the methoxyl group during decarboxylation. The best yields were obtained by partial hydrolysis of the ester (VI) to the corresponding half-ester, followed by decarboxylation under reduced pressure; from the resulting mixture of ethyl 3-methoxy-2-propylpentanoate (VII; R = Et) with the unsaturated ester arising by elimination of the methoxyl group the unsaturated ester was removed by oxidation with potassium permanganate in acetone. Alkaline hydrolysis of the methoxy-ester (VII; R = Et) readily gave the corresponding acid (VII; R = H).

The conversion of this acid into its chloride was then investigated. Reaction of the acid with thionyl chloride in benzene solution resulted in removal of the methoxyl group, which also occurred when nitrogen was passed through the solution (in order to remove hydrogen chloride) during the preparation of the acid chloride. The methoxy-acid chloride was, however, readily obtained by treatment of the acid with thionyl chloride in the presence of pyridine.

(IV) $Cl\cdot[CH_2]_2\cdot CHCl\cdot OMe$

(V) $Cl\cdot[CH_2]_2\cdot CH(OMe)\cdot C(CO_2Et)_2$, $[CH_2]_3\cdot CH_3$

$CH_3\cdot CH_2\cdot CH(OMe)\cdot C(CO_2Et)_2$, $[CH_2]_3\cdot CH_3$ (VI)

$CH_3\cdot CH_2\cdot CH(OMe)\cdot CH\cdot CO_2R$, $[CH_2]_3\cdot CH_3$ (VII)

The next step was the reaction of the acid chloride with an alkyl-substituted malonic ester by Bowman and Fordham's procedure;[3] octadecylmalonic ester was chosen as a model. Accordingly, the latter was converted by partial hydrolysis into ethyl hydrogen octadecylmalonate, and thence, by reaction with 2 : 3-dihydropyran in the presence of toluene-*p*-sulphonic acid, into ethyl tetrahydro-2-pyranyl octadecylmalonate (VIII; Py = tetrahydro-2-pyranyl). The sodio-derivative of this malonic ester on condensation with the chloride derived from the acid (VII; R = H) afforded the keto-ester (IX) which,

(VIII) $PyO_2C\cdot CH\cdot CO_2Et$, $[CH_2]_{17}\cdot CH_3$

$CH_3\cdot CH_2\cdot CH(OMe)\cdot CH\cdot CH(OH)\cdot CH\cdot CO_2Et$ (X)
$CH_2\cdot[CH_2]_2$ $[CH_2]_{17}\cdot CH_3$

(IX) $CH_3\cdot CH_2\cdot CH(OMe)\cdot CH{-}CO{-}CH\cdot CO_2Et$
$CH_2\cdot[CH_2]_2$ $[CH_2]_{17}\cdot CH_3$

without purification, was reduced directly with sodium borohydride. Chromatography of the product over alumina afforded ethyl 2-(1-hydroxy-3-methoxy-2-propylpentyl)-eicosanoate (X).

It is of interest to note that the infrared spectrum (Nujol) of the ester (X), possessing

[5] Hill and Keach, *J. Amer. Chem. Soc.*, 1926, **48**, 257.
[6] Duliere, *Bull. Soc. chim. France*, 1923, **33**, 1647.
[7] Henze, Benz, and Sutherland, *J. Amer. Chem. Soc.*, 1949, **71**, 2122.

a secondary methoxyl group, shows the methoxyl band at 1093 cm.$^{-1}$ in agreement with that of methyl mycolate. As already pointed out,[8] there appears to be a difference in the position of this band between aliphatic compounds with a secondary and those with a tertiary methoxyl group.

Experimental

Ethyl 2-Methyl-3-oxoeicosanoate (II).—The procedure of Bowman and Fordham[3] was followed. Concentrated sulphuric acid (10 drops) was added to a solution of 2 : 3-dihydropyran (63 g.; purified by refluxing over sodium, and distillation) in dry benzene (500 c.c.), and then ethyl hydrogen methylmalonate[9] (73 g.) in benzene (500 c.c.) was introduced at <30°. After a further hr., traces of acid were removed by stirring the mixture with potassium hydroxide (30 g.) for 0·5 hr. The benzene solution was then decanted, and benzene and excess of dihydropyran were removed under reduced pressure (bath temperature <30°), to give ethyl tetrahydro-2-pyranyl methylmalonate. This ester (46 g.) was converted into its sodio-derivative by adding it in benzene (150 c.c.) with cooling (<35°) to powdered sodium (4·8 g.) and benzene (300 c.c.). When all the sodium had dissolved, a solution of stearoyl chloride (60·5 g.; obtained from stearic acid, m. p. 69—69·5°, by means of thionyl chloride) in benzene (200 c.c.) was added with stirring. After a further 0·5 hour's stirring, acetic acid (20 c.c.) was added and the mixture refluxed for several hr. (to complete the decarboxylation), then poured into water. The benzene layer, after being concentrated, deposited on cooling stearic acid which was filtered off. The remaining solution was diluted with light petroleum (b. p. 80—100°) and shaken with 1% aqueous-methanolic (1 : 1) sodium hydroxide in order to remove the remaining stearic acid. Evaporation of the benzene–petroleum solution gave *ethyl 2-methyl-3-oxoeicosanoate* (16·8 g.), m. p. 40—41° (from ethanol) (Found: C, 75·1; H, 11·9. $C_{23}H_{44}O_3$ requires C, 75·0; H, 12·0%).

Ethyl 3-Hydroxy-2-methyleicosanoate (III).—The above oxo-ester (11 g.) was hydrogenated in ethanol (150 c.c.) in the presence of triethylamine[10] (1 c.c.) with Raney nickel (W-2) at 125 atm./100° in 5 hr. (cf. ref. 4). Evaporation of the filtered solution gave *ethyl 3-hydroxy-2-methyleicosanoate*, m. p. 43—44·5° (from ethanol) (Found: C, 74·4; H, 12·5. $C_{23}H_{46}O_3$ requires C, 74·5; H, 12·5%).

Attempted O-Methylation of Ethyl 3-Hydroxy-2-methyleicosanoate.—(i) The hydroxy-ester (10·6 g.) was refluxed with methyl iodide (80 g.) and silver oxide (13 g.; added in small portions) for 8 hr. On isolation of the product unchanged hydroxy-ester was obtained.

(ii) The hydroxy-ester (0·5 g.) in benzene (20 c.c.) was added to powdered potassium (0·4 g.) under benzene (25 c.c.), and the mixture refluxed for 1 hr.; methyl iodide (20 c.c.) was then added and the refluxing continued for another 3 hr. The product was an oil which showed $\lambda_{max.}$ 2120 Å (ε 3625 in *cyclo*hexane). The procedure was repeated in a similar way, except that the mixture was refluxed with potassium for only 15 min., then refluxed with methyl iodide for 15 min.; the product (Found: C, 81·5; H, 13·3%) contained, according to its infrared spectrum, no hydroxyl and little methoxyl.

(iii) The hydroxy-ester (0·5 g.) was heated on a steam-bath with sodium hydride (1 g.) in ethylene glycol diethyl ether (10 c.c.) for 5 min., methyl iodide (15 c.c.) was then added, and the whole refluxed for 10 min. The product obtained on acidification was a complex mixture containing unsaturated material; its infrared spectrum showed no strong methoxyl band.

(iv) The hydroxy-ester was recovered unchanged after being treated in ethereal solution with sodamide and dimethyl sulphate.

(v) The hydroxy-ester (0·4 g.) was heated on a steam-bath with red phosphorus (24 mg.) and iodine (0·25 g.) for 3 hr. The product was extracted with ether, and to the ethereal extract a solution of sodium (46 mg.) in methanol (1 c.c.) was added; a precipitate of sodium iodide resulted. The mixture was shaken with water, and the ethereal layer dried ($MgSO_4$) and evaporated. The residue was according to its infrared spectrum a mixture of αβ-unsaturated acid and ester; there was no evidence of the presence of methoxyl.

Ethyl 2-Ethoxycarbonyl-3-methoxy-2-propylpentanoate (VI).—Ethyl propylmalonate (40·4 g.) was introduced slowly, with stirring, on to sodium (4·6 g.; small pieces) under ether (100 c.c.). When all the sodium had dissolved, freshly prepared 1-chloropropyl methyl ether[7] (27·5 g.;

[8] Lewis and Polgar, *J.*, 1958, 102.
[9] Breslow, Baumgarten, and Hauser, *J. Amer. Chem. Soc.*, 1944, **66**, 1287.
[10] Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 695.

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b. p. 44°/100 mm.) in benzene–ether (1 : 1) was added quickly (vigorous reaction). The mixture was refluxed with stirring for 0·5 hr., then acidified (glacial acetic acid), diluted with water, and extracted with ether. Distillation gave *ethyl 2-ethoxycarbonyl-3-methoxy-2-propylpentanoate* (35·9 g.), b. p. 136—140°/11 mm., n_D^{18} 1·4360 (Found: C, 61·3; H, 9·45. $C_{14}H_{26}O_5$ requires C, 61·3; H, 9·55%).

Ethyl 5-Chloro-2-ethoxycarbonyl-3-methoxy-2-propylpentanoate (V).—1 : 3-Dichloropropyl methyl ether [6] (36·9 g.; b. p. 50—52°/19 mm.) was condensed with ethyl sodiopropylmalonate (from 44·5 g. of ethyl propylmalonate and 5·05 g. of sodium in 50 c.c. of ether) in the manner described in the preceding section. Isolation of the product as above gave *ethyl 5-chloro-2-ethoxycarbonyl-3-methoxy-2-propylpentanoate* (37·3 g.), b. p. 140—145°/1 mm., n_D^{20} 1·4460 (Found: C, 55·7; H, 8·1. $C_{14}H_{25}O_5Cl$ requires C, 55·4; H, 8·15%). Reduction of this chloro-ester by refluxing it with zinc amalgam (150 g.) and glacial acetic acid (500 c.c.) for 24 hr. gave ethyl 2-ethoxycarbonyl-3-methoxy-2-propylpentanoate (VI), b. p. 150—160°/19 mm., n_D^{16} 1·4355 (Found: C, 61·0; H, 9·3%), together with *ethyl 3-acetoxy-2-ethoxycarbonyl-2-propylpentanoate*, b. p. 190—194°/19 mm., n_D^{18} 1·4510 (Found: C, 59·6; H, 9·0. $C_{15}H_{26}O_6$ requires C, 59·6; H, 8·7%); the latter arose by replacement of the methoxyl group by acetoxyl.

3-Methoxy-2-propylpentanoic Acid (VII; R = H).—Ethyl 2-ethoxycarbonyl-3-methoxy-2-propylpentanoate (33·5 g.) was refluxed with potassium hydroxide (7·9 g.) in ethanol (150 c.c.) for 4 hr. After acidification with dilute hydrochloric acid, the mixture was extracted with ether, and the ethereal solution re-extracted with 5% aqueous sodium hydroxide. Acidification of the aqueous phase gave the acidic fraction (half-ester, together with some di-acid) which was collected with ether, then decarboxylated by distillation under reduced pressure. The product was taken up in ether, washed with 5% aqueous sodium hydroxide (to remove acidic material arising by decarboxylation of the di-acid), then distilled, to give the crude ethyl ester (19·7 g.), b. p. 100—110°/12 mm., n_D^{19} 1·4295 (the infrared and ultraviolet spectra showed the presence of some αβ-unsaturated material). Powdered potassium permanganate was added to a refluxing solution of this ester (18 g.) in acetone (100 c.c.) in portions until the rate of oxidation became very slow; the mixture was then set aside with a slight excess of potassium permanganate for 2 hr. After addition of sodium hydrogen sulphite and dilute hydrochloric acid, the mixture was extracted with ether. Distillation of the dried ($MgSO_4$) extract gave *ethyl 3-methoxy-2-propylpentanoate* (12·7 g.), b. p. 100—110°/12 mm., n_D^{19} 1·4222 (Found: C, 64·9; H, 10·8. $C_{11}H_{22}O_3$ requires C, 65·2; H, 11·0%). This ester was hydrolysed by refluxing 5% aqueous-ethanolic (1 : 1) potassium hydroxide for 4 hr. Unhydrolysed ester was removed by ether-extraction, and the aqueous phase acidified with dilute hydrochloric acid, then extracted with ether. After being washed with water until the washings were neutral to litmus, the ethereal solution was distilled, to give *3-methoxy-2-propylpentanoic acid*, b. p. 142—145°/16 mm., n_D^{19} 1·4352 (Found: C, 61·7; H, 10·2. $C_9H_{18}O_3$ requires C, 62·0; H, 10·4%). The *amide*, prepared *via* the acid chloride, itself obtained by means of thionyl chloride in the presence of pyridine (see following section), crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 72—73° (Found: C, 62·7; H, 10·9. $C_9H_{19}O_2N$ requires C, 62·5; H, 11·0%). When a benzene solution of the acid was refluxed with thionyl chloride, the resulting acid chloride gave with ammonia an amide, m. p. 113—113·5° (from ethanol) (Found: C, 68·2; H, 10·5; N, 9·7. Calc. for $C_9H_{15}ON$: C, 68·0; H, 10·7; N, 9·9%), loss of the elements of methanol having taken place; Macq [11] gives m. p. 115·5° for the higher-melting isomer of 2-propylpent-2-enamide.

Ethyl 2-(1-Hydroxy-3-methoxy-2-propylpentyl)eicosanoate (X).—Ethyl octadecylmalonate (b. p. 198—200°/0·3 mm.; prepared from octadecyl iodide and ethyl sodiomalonate in the usual manner) was converted, by the procedure given by Breslow *et al.*[9] for the preparation of ethyl hydrogen methylmalonate, into ethyl hydrogen octadecylmalonate, m. p. 61—62° (Found: C, 71·6; H, 11·4. Calc. for $C_{23}H_{44}O_4$: C, 71·8; H, 11·5%). This reacted with 2 : 3-dihydropyran in the presence of toluene-*p*-sulphonic acid (cf. Bowman and Fordham [3]), affording ethyl tetrahydro-2-pyranyl octadecylmalonate, m. p. 59—60° (decomp.) (crude product).

Thionyl chloride (2·15 c.c.) in benzene (5 c.c.) was added with stirring to a solution of 3-methoxy-2-propylpentanoic acid (3·9 g.) and pyridine (2·5 g.) in benzene (10 c.c.), cooled in an ice-bath; the mixture was left at 0° for 30 min., and at room temperature for another 30 min. The benzene was then removed under reduced pressure at room temperature. The resulting crude acid chloride was condensed with ethyl tetrahydro-2-pyranyl octadecylsodiomalonate

[11] Macq, *Bull. Acad. roy. Belg., Cl. Sci., Ser* 5, 1926, **12**, 753; *Chem. Zentr.*, 1927, I, 880.

(from 9·9 g. of the malonic ester and 0·54 g. of sodium in 100 c.c. of benzene) according to the general procedure.[3] The mixture was worked up as described,[3] except that the resulting material was heated at 130°/0·4 mm. to remove volatile substances. The crude oxo-ester (4·5 g.) so obtained was dissolved in ethanol, and a suspension of sodium borohydride (0·5 g.) in ethanol–water (9 : 1, 20 c.c.) was added carefully. The mixture was set aside for 1 hr., then 5% aqueous sodium hydroxide was added to decompose the borate complex. The organic material was extracted with ether, and the extract washed with dilute hydrochloric acid and water, then dried ($MgSO_4$) and evaporated. The residue was chromatographed in light petroleum (b. p. 40—60°) on alumina (Spence, type H; activity III on the scale of Brockmann and Schodder [12]). Elution with light petroleum gave fractions containing some ethyl eicosanoate and unsaturated material. Further elution with benzene and benzene–ether gave *ethyl 2-(1-hydroxy-3-methoxy-2-propylpentyl)eicosanoate*, m. p. 63—65° after crystallisation from light petroleum (b. p. 40—60°) (Found: C, 74·6; H, 12·3. $C_{31}H_{62}O_4$ requires C, 74·7; H, 12·5%).

This work was carried out during the tenure of an Imperial Oil Graduate Research Fellowship (by E. D. M.).

Dyson Perrins Laboratory, Oxford University. [*Received, July 11th*, 1958.]

[12] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.

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821. *Organophosphorus Compounds of Sulphur and Selenium. Part X.* Action of Sulphuryl Chloride on Alkyl Hydrogen Alkylphosphonothioates and Dialkylphosphinothioic Acids. Synthesis of* P-*Alkoxy*-P-*alkyloxophosphoranesulphenyl Chlorides.*

By Cz. Borecki, J. Michalski, and St. Musierowicz.

Reaction of sulphuryl chloride with alkyl hydrogen alkylphosphonothioates leads to *P*-alkoxy-*P*-alkyloxophosphoranesulphenyl chlorides or bis(alkoxyalkylphosphinyl) disulphides, depending on the amount of reagent used. The products are thermally unstable and yield on decomposition alkyl alkylphosphonochloridates or thionoanhydrides.

Dialkylphosphinothioic acids with sulphuryl chloride give dialkylphosphinyl chlorides or the thionoanhydrides.

Earlier reports [1] from this laboratory described a new type of organophosphorus compounds, namely, dialkoxyoxophosphoranesulphenyl chlorides, $(RO)_2PO{\cdot}SCl$.† Some *P*-alkoxy-*P*-alkyl- (II) and dialkyl-oxophosphoranesulphenyl chlorides $R_2PO{\cdot}SCl$ have now been investigated. Although only the compounds (II) have been isolated, the remaining results appear worth reporting.

The method used previously for preparing dialkoxyoxophosphoranesulphenyl chlorides involved treatment of dialkylphosphorothioates $(RO)_2PS{\cdot}OH$ or bis(dialkoxyphosphinyl) disulphides $[(RO)_2PO{\cdot}S]_2$ with chlorine or, more conveniently, sulphuryl chloride.[1] When sulphuryl chloride and *O*-alkyl hydrogen alkylphosphonothioates (I) (prepared from alkyl hydrogen alkylphosphonites [2]) were used in equimolar proportions, the sulphenyl chlorides (II) were formed. When the amount of chlorinating agent used was halved, bis(alkoxyalkylphosphinyl) disulphides (III) were produced; these were readily converted

* Part IX, *Roczniki Chem.*, in the press.

† This and similar nomenclature is based on the hypothetical parent compound, phosphorane PH_5 (*J.*, 1952, 5122), and the radical phosphenyl $PH_2(O)$–.

[1] Lenard and Michalski, *Roczniki Chem.*, 1956, **30**, 655; Lenard-Borecka and Michalski, *ibid.*, 1957, **31**, 1269; Michalski, Lenard-Borecka, Musierowicz, and Skowronska, XVIth Internat. Congr. Pure Appl. Chem., Paris, 1957, Handbook Vol. II, p. 108.

[2] Michalski and Skowronska, *Roczniki Chem.*, 1956, **30**, 799.

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into the chlorides (II) by sulphuryl chloride. The disulphides (III) were also obtained by condensation of the acids (I) with the chlorides (II) (reaction *b*).

$$\underset{\text{(I)}}{R(RO)PS{\cdot}OH} + SO_2Cl_2 \longrightarrow \underset{\text{(II)}}{RPO(OR){\cdot}SCl} + HCl + SO_2 \quad . \quad . \quad . \quad . \quad . \quad (a)$$

$$RPO(OR){\cdot}SCl + HOSP(OR)R \longrightarrow \underset{\text{(III)}}{[RPO(OR){\cdot}S{\cdot}]_2} + HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (b)$$

$$[RPO(OR){\cdot}S{\cdot}]_2 + SO_2Cl_2 \longrightarrow 2RPO(OR){\cdot}SCl + SO_2$$

The yields of chloride (II), isolated by distillation, were lower than expected (30—70%), owing to thermal decomposition which was very fast at 80° but required a few days at room temperature:

$$RPO(OR){\cdot}SCl \longrightarrow S + RPO(OR)Cl \text{ (IV)}$$

The alkyl alkylphosphonochloridates (IV) formed agreed in properties with those obtained from alkyl hydrogen alkylphosphonites.[2] The disulphides (III) were also unstable, decomposing rapidly at 100° and within several days at room temperature, to yield sulphur and the alkoxyalkylphosphinyl alkoxyalkylphosphinothioyl anhydrides (V):

$$[RPO(OR){\cdot}S{\cdot}]_2 \longrightarrow S + RPS(OR){\cdot}O{\cdot}PRO(OR) \text{ (V)}$$

The structure of these products (V) was confirmed by comparing their properties with those of compounds obtained by action of hydrogen sulphide on alkyl alkylphosphonochloridates (IV) in the presence of tertiary bases.[3] The infrared spectra of compounds (V) prepared by the latter route indicate the thiono-structure shown.[4]

The action of sulphuryl chloride on dialkylphosphinothioic acids $R_2PS{\cdot}OH$ failed, however to yield dialkyloxophosphoranesulphenyl chlorides $R_2PO{\cdot}SCl$. For reasons given below it is probable that these chlorides were in fact formed but were too unstable to be isolated.

Our investigations were concerned with diethylphosphinothioic acid $Et_2PS{\cdot}OH$ [obtained by alkaline hydrolysis of diethylphosphinothioyl chloride $Et_2P(S)Cl$] and with dibenzylphosphinothioic acid [prepared by adding sulphur to dibenzylphosphine oxide $(Ph{\cdot}CH_2)_2PHO$]. Chlorination of acids $R_2PS{\cdot}OH$ was carried out under conditions analogous to those used for acids (I).

Sulphuryl chloride and diethylphosphinothioic acid in equimolar proportions afford diethylphosphinyl chloride (VI) in good yield:

$$Et_2PS{\cdot}OH + SO_2Cl_2 \longrightarrow S + HCl + SO_2 + Et_2P(O){\cdot}Cl \text{ (VI)}$$

Reaction of diphenylphosphinothioic acid [5] is similar. Reaction with 0·5 mol. of sulphuryl chloride yields the anhydride (VII):

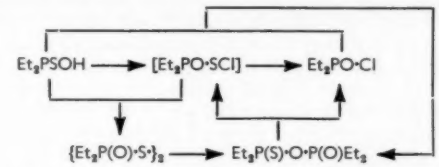
$$2Et_2PS{\cdot}OH + SO_2Cl_2 \longrightarrow S + 2HCl + SO_2 + Et_2P(S){\cdot}O{\cdot}P(O)Et_2 \text{ (VII)}$$

In both these cases elemental sulphur is formed. Liberation of sulphur is evident even at 0° and is very rapid at room temperature.

These facts, analogy with the chlorination of thioacids of phosphorus investigated earlier, and additional observations reported below make it legitimate to propose the annexed scheme. According to this the thioanhydride (VII) may be produced either by decomposition of the disulphide or by condensation of diethylphosphinyl chloride with diethylphosphinothioic acid, this chloride being produced by decomposition of the unstable sulphenyl chloride, and the disulphide by condensation of the sulphenyl chloride with diethylphosphinothioic acid. In the final stage of the reaction, the thioanhydride decomposes to sulphur and diethylphosphinyl chloride. The last reaction also appears

[3] Michalski, *ibid.*, 1955, **29**, 960.
[4] Coe, Perry, and Brown, *J.*, 1957, 3604.
[5] Craig, U.S.P. 2,724,726.

to proceed in two stages. In the first, one molecule each of diethylphosphinyl chloride and the sulphenyl chloride are produced; in the second the latter chloride decomposes to



diethylphosphinyl chloride and sulphur. In conformity with the proposed scheme diethylphosphinothioic acid was found to condense with diethylphosphinyl chloride:

$$Et_2PO{\cdot}Cl + HO{\cdot}PSEt_2 \longrightarrow Et_2P(S){\cdot}O{\cdot}P(O)Et_2 + HCl$$

and the thioanhydride with sulphuryl chloride gave diethylphosphinyl chloride:

$$Et_2P(S){\cdot}O{\cdot}P(O)Et_2 + SO_2Cl_2 \longrightarrow 2Et_2PO{\cdot}Cl + SO_2 + S$$

Both reactions have general implications in respect of the system $>P(S){\cdot}OP(O)<$ and will be investigated further.

The thioanhydride (VII) obtained in the reactions referred to above proved identical with that systhesized earlier [2] by treating diethylphosphinyl chloride with hydrogen sulphide in the presence of tertiary amines. We ascribe to it a structure with thionic sulphur linkage, in analogy with the compounds (V) and the thiopyrophosphates.

Sulphuryl chloride and dibenzylphosphinothioic acid afford dibenzylphosphinyl chloride and sulphur:

$$(Ph{\cdot}CH_2)_2PS{\cdot}OH + SO_2Cl_2 \longrightarrow (Ph{\cdot}CH_2)_2PO{\cdot}Cl + S + SO_2 + HCl$$

When 0·5 mol. of sulphuryl chloride was used, no secondary reactions were noted and unchanged dibenzylphosphinothioic acid was present. Observation of the reactions presents some difficulties owing to the susceptibility of dibenzylphosphinyl chloride to hydrolysis. These experiments do not warrant any conclusions as to the course of secondary processes resembling those noted for the diethyl analogue. They confirm, however, the instability of group $>PO{\cdot}SCl$ combined with two radicals by direct phosphorus–carbon links. The stability of the system decreases as alkoxy-groups are replaced by alkyl.

Experimental

Extracts were dried over $MgSO_4$. Carbon was determined by McCready and Hassid's procedure.[6]

P-*Ethoxy*-P-*ethyloxophosphoranesulphenyl Chloride*.—Sulphuryl chloride (27 g.) in benzene (30 ml.) was added dropwise to a solution of ethyl ethylphosphonothioic acid [2] (30·8 g.) in benzene (100 ml.). Reaction was exothermic but the temperature was kept at −5° to 0°. The solvent and gaseous products were removed under reduced pressure. The *sulphenyl chloride* was distilled *in vacuo* as a yellow liquid (26 g., 70%), b. p. 33—34°/0·5 mm., n_D^{20} 1·4800, d_4^{20} 1·2312 (Found: P, 15·9; Cl, 18·7. $C_4H_{10}O_2ClSP$ requires P, 16·4; Cl, 18·8%).

n-*Butyl Hydrogen Ethylphosphonothioate*.[7,2]—*n*-Butyl hydrogen ethylphosphonite [2] (74·3 g.) was added to a solution from sodium (11 g.) in anhydrous *n*-butyl alcohol (150 ml.). Sulphur (15 g.) was added slowly with cooling. Unchanged sulphur was then filtered off, the filtrate evaporated *in vacuo* to dryness, and the crude sodium salt dissolved in water (50 ml.) and acidified with 20% hydrochloric acid (90 ml.). The free acid was extracted with benzene (3 × 70 ml.). The extracts were evaporated *in vacuo* and distillation of the residue gave n-*butyl hydrogen ethylphosphonothioate* (51·5 g., 56%), b. p. 76°/0·06 mm., n_D^{25} 1·4821, d_4^{25} 1·0683 (Found: P, 16·9. $C_6H_{15}O_2SP$ requires P, 17·0%).

P-n-*Butoxy*-P-*ethyloxophosphoranesulphenyl Chloride*.—Sulphuryl chloride (13·5 g.) in

[6] McCready and Hassid, *Ind. Eng. Chem. Anal.*, 1942, **14**, 526.

[7] Foss, *Acta Chem. Scand.*, 1947, **1**, 8; Kabachnik, Kurochkin, Mastryukova, Joffe, Popov, and Rodionova, *Doklady Akad. Nauk S.S.S.R.*, 1955, **104**, 861.

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benzene (40 ml.) was added dropwise to *n*-butyl hydrogen ethylphosphonothioate (18 g.) diluted with benzene (60 ml.). The temperature of the exothermic reaction was kept at −10° to −5°. The solvent was evaporated and the *sulphenyl chloride* distilled *in vacuo* as a yellow liquid (11·8 g., 55%), b. p. 74°/0·4 mm., n_D^{25} 1·4528 (Found: P, 14·7. $C_6H_{14}O_2ClSP$ requires P, 14·3%).

Thermal Decomposition of P-*Ethoxy*-P-*ethyloxophosphoranesulphenyl Chloride.—Ethyl ethylphosphonochloridate.* The chloride (26·4 g.) was heated in a vacuum-still at 60—70°/*ca.* 1 mm. Precipitation of sulphur and distillation were observed. The ethyl ethylphosphonochloridate formed (15·5 g., 71%) was distilled *in vacuo*, having b. p. 35—36°/0·2 mm., n_D^{20} 1·4402 (Found: P, 19·6; Cl, 22·5. Calc. for $C_4H_{10}O_2ClP$: P, 19·7; Cl, 22·6%). Michalski and Skowronska [2] give b. p. 53—54°/1 mm., n_D^{25} 1·4378.

Bis-(P-*ethoxy*-P-*ethylphosphinyl*) *Disulphide.*—(i) Sulphuryl chloride (5·15 g.) in benzene (20 ml.) was added dropwise to ethyl hydrogen ethylphosphonothioate (11·75 g.) in benzene (60 ml.) at 0°. The solvent and gaseous products were removed *in vacuo* and the residue gave the *disulphide* as a pale yellow oil (11·7 g., 98%), n_D^{26} 1·5061 (Found: P, 20·7. $C_8H_{20}O_4S_2P_2$ requires P, 20·2%).

(ii) Ethoxyethyloxophosphoranesulphenyl chloride (9·47 g.) in benzene (100 ml.) was added dropwise to ethyl hydrogen ethylphosphonothioate (7·79 g.) in benzene (70 ml.) at −5° to 0°. The solvent and gaseous products were removed *in vacuo* and the residue gave the disulphide (15·2 g., 98%), n_D^{20} 1·5051 (Found: P, 20·2%).

Thermal Decomposition of Bis(ethoxyethylphosphinyl) Disulphide.—The disulphide (15·2 g.) was heated at 120°/*ca.* 0·05 mm. The crude anhydride (VII) which collected distilled as a pale yellow oil (10·2 g., 75%), b. p. 74—75°/0·05 mm., n_D^{25} 1·4744 (Found: P, 22·3. Calc. for $C_8H_{20}O_4SP_2$: P, 22·6%). Michalski and Skowronska [2] give b. p. 119—120°/0·8 mm., n_D^{25} 1·4652.

Diethylphosphinothioyl Chloride.—Sulphur (16·2 g.) was added portionwise to diethylchlorophosphine [9] (63·5 g.) in benzene (250 ml.) at 18—24°. The solvent was evaporated and the crude *diethylphosphinothioyl chloride* distilled as a colourless liquid (70·8 g., 89%), b. p. 94—95°/9 mm., n_D^{25} 1·5292 (Found: P, 19·8; Cl, 22·1. $C_4H_{10}ClSP$ requires P, 19·8; Cl, 22·6%).

Diethylphosphinothioic Acid.—An aqueous solution of sodium hydroxide (25 g. in 50 ml.) was added dropwise to diethylphosphinothioyl chloride (45 g.) at 30—40°. The resulting aqueous solution of sodium diethylphosphinothioate was acidified with 20% hydrochloric acid. *Diethylphosphinothioic acid* which separated was added to a benzene extract of the aqueous layer (3 × 50 ml.). The solvent was evaporated and the crude acid distilled as a colourless liquid (31 g., 78%), b. p. 67—68°/0·12 mm., n_D^{25} 1·5257 (Found: P, 22·3. $C_4H_{11}OSP$ requires P, 22·4%). The cyclo*hexylamine salt*, prepared in usual way, formed needles (from benzene), m. p. 145—147° (Found: P, 13·1; N, 5·9. $C_{10}H_{24}ONPS$ requires P, 13·1; N, 5·9%). The compound with m. p. 76° claimed by Strecker and Grosmann [10] as diethylphosphinothioic acid probably has a different structure.[11]

Action of Sulphuryl Chloride on Diethylphosphinothioic Acid.—(i) Sulphuryl chloride (14·6 g., 1 mol.) in benzene (50 ml.) was added dropwise to diethylphosphinothioic acid (15 g., 1 mol.) in benzene (50 ml.), the temperature being kept at −6° to −2°. Sulphur was precipitated. The solvent was evaporated and the diethylphosphinyl chloride was distilled as a colourless liquid (10·2 g., 61%), b. p. 96—98°/10 mm., n_D^{20} 1·4682 (Found: P, 21·8; Cl, 25·1. Calc. for $C_4H_{10}OPCl$: P, 22·3; Cl, 25·2%). Razumov, Mukhacheva, and Zaikonnikova [12] give b. p. 108—109·5°/16 mm., n_D^{20} 1·4647.

(ii) Sulphuryl chloride (6·5 g., 0·5 mol.) in benzene (20 ml.) was added dropwise to diethylphosphinothioic acid (13·4 g., 1 mol.) in benzene (30 ml.) at 0°. The mixture was then left for 1 hr. at room temperature. The precipitated sulphur was filtered off, and the thioanhydride distilled as a pale yellow oil (6·9 g., 59%), b. p. 94—95°/0·07 mm., n_D^{20} 1·5030 (Found: P, 25·6. Calc. for $C_8H_{20}O_2SP_2$: P, 25·6%). Michalski [2] gives b. p. 140°/0·5 mm., n_D^{25} 1·5056.

Condensation of Diethylphosphinyl Chloride with Diethylphosphinothioic Acid.—The acid (8 g.) in benzene (8 ml.) was added dropwise to the chloride (8·1 g.) in benzene (7 ml.) at 15—20°. Hydrogen chloride and solvent were removed under reduced pressure. Diethylphosphinic diethylphosphinothionic anhydride distilled as a pale yellow oil (12·4 g., 96%), b. p. 93—94°/0·05 mm., n_D^{20} 1·5037 (Found: P, 25·4. Calc. for $C_8H_{20}O_2SP_2$: P, 25·6%).

[9] Beeby and Mann, *J.*, 1951, 413.
[10] Strecker and Grosmann, *Ber.*, 1916, **49**, 63.
[11] Kabachnik and Shepeleva, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1949, 56.
[12] Razumov, Mukhacheva, and Zaikonnikova, *Zhur. obshchei Khim.*, 1957, **27**, 754.

Action of Sulphuryl Chloride on the Preceding Anhydride.—Sulphuryl chloride (2·1 g.) in benzene (10 ml.) was added dropwise to the anhydride (3·7 g.) in benzene (10 ml.) at −2° to 0°. Precipitated sulphur was filtered off, and solvent evaporated. Diethylphosphinic chloride distilled as a colourless liquid (2·1 g., 48%), b. p. 104°/13 mm., n_D^{25} 1·4668 (Found: P, 22·3. Calc. for $C_4H_{10}OClP$: P, 22·3%).

Dibenzylphosphinothioic Acid.—To an alcoholic solution of sodium ethoxide (obtained from 3·35 g. of sodium in 100 ml. of ethanol) dibenzylphosphine oxide [13] (33 g.) in ethanol (200 ml.) was added. The mixture was stirred while sulphur (5·2 g.) was added portionwise at 30—35°. Stirring was continued for a further 2 hr. Excess of sulphur was filtered off, and the solvent evaporated at reduced pressure. *Sodium dibenzylphosphinothioate* crystallized from ethanol as needles, m. p. 232—236° (Found: P, 10·5. $C_{14}H_{14}OSPNa$ requires P, 10·9%). This salt (31 g.) was dissolved in water (200 ml.) and decomposed by excess of hydrochloric acid at 0°. The *dibenzylphosphinothioic acid* which separated crystallized from ethanol–benzene (1 : 10) as colourless plates, m. p. 190—191°, slightly soluble in benzene and carbon tetrachloride (Found: C, 64·3; S, 11·9. $C_{14}H_{15}OSP$ requires C, 64·1; S, 12·2%). The compound with m. p. 171° claimed by Strecker and Grosmann [10] as dibenzylphosphinothioic acid has probably a different structure.[11]

Action of Sulphuryl Chloride on Dibenzylphosphinothioic Acid.—Sulphuryl chloride (2·7 g., 1 mol.) dissolved in benzene (30 ml.) was added dropwise to a suspension of dibenzylphosphinothioic acid (5·24 g., 1 mol.) in carbon tetrachloride (120 ml.) −25° to −20°. The solid disappeared. When the solvent was evaporated under reduced pressure at 0°, sulphur was precipitated. This was filtered off. The dibenzylphosphinyl chloride present in the filtrate was difficult to purify owing to pronounced instability and was hydrolysed by a few drops of water to the dibenzylphosphinic acid. The product crystallized from benzene as plates, m. p. 191—193° (Found: C, 68·4. Calc. for $C_{14}H_{15}O_2P$: C, 68·3%). The acid showed no m. p. depression when mixed with a sample of acid prepared by Miller, Bradley, and Hamilton's method.[13]

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Department of Organic Chemistry, Technical University (Politechnika), Lodz, Poland. [*Received, April 24th*, 1958.

[13] Miller, Bradley, and Hamilton, *J. Amer. Chem. Soc.*, 1956, **78**, 5299.

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822. *The Benzoylation of Substituted Anilines in Different Solvents.*

By A. N. Bose and Sir Cyril Hinshelwood.

The bimolecular rate constants (k) and activation energies (E) have been measured for the benzoylation of various mono- and di-substituted anilines in nitrobenzene and some other polar solvents. Changes in rate with substitution are mainly due to changes in E. In nitrobenzene the activation energy is uniformly lower than in benzene, the effect being partially compensated by a lower value of the pre-exponential factor of the Arrhenius equation.

There is a linear relation between log k and log K (K = basic dissociation constant in water). The slope of the line is the same for the reactions in nitrobenzene and in benzene, showing that a highly polar solvent does not affect the transmission of the electronic influence of the substituent to the nitrogen atom.

In most examples the changes in activation energy caused by two substituents are nearly additive.

The kinetics of the benzoylation of substituted anilines in benzene were systematically studied by Stubbs and Hinshelwood.[1] For this reaction (*a*) the entropy of activation

[1] Stubbs and Hinshelwood, *J.*, 1949, S71.

XUM

remains very nearly constant, (*b*) the resultant effect on the activation energy of two substituents in the same benzene nucleus of the amine is approximately the sum of their individual effects, and (*c*) there is a functional relationship between the reactivity of the mono-derivatives and the polarity of the substituent or the dissociation constant of the amine.

We now extend the work to polar solvents. The kinetics of benzoylation of eighteen substituted anilines in nitrobenzene were studied to find out (*a*) whether the entropy of activation in this solvent also is constant, (*b*) whether the plot of $\log_{10}k$ (in the solvent) against the logarithm of the dissociation constant of the amine (in water) is a line of the same slope as for benzene or whether the highly polar solvents affect the transmission of the influence of the substituent, (*c*) how the energy of activation and the frequency factor of the reaction are affected when the solvent is changed, and (*d*) whether the additive effect of the substituents still holds as it does in benzene.

The kinetics of benzoylation of eight substituted anilines in chlorobenzene, bromobenzene, toluene, and phenyl cyanide were also studied to see how the rate depends on the dipole moment of the solvent.

Experimental

Aniline is benzoylated quantitatively according to the equations $Ph{\cdot}COCl + Ph{\cdot}NH_2 = Ph{\cdot}NH{\cdot}COPh + HCl$ (slow); $Ph{\cdot}NH_2 + HCl = Ph{\cdot}NH_2{,}HCl$ (rapid). The aniline hydrochloride was filtered off and dissolved in water, the chloride being estimated by Volhard's method. This procedure proved satisfactory for the reaction in toluene, chlorobenzene, and bromobenzene but with phenyl cyanide and nitrobenzene, in which the hydrochloride is slightly soluble, the reaction mixture was cooled to $-20°$ and excess of benzene was added; the complete precipitation of the hydrochloride in these conditions was confirmed by the fact that the method gave the theoretical end point for the reaction.

In most of the experiments the concentrations of the reaction mixture were 0·01M-aniline and 0·005M-benzoyl chloride (dilution I). For some of the substituted anilines in nitrobenzene dilution I was unsuitable since the hydrochloride was not precipitated completely even after cooling and addition of benzene, so the concentrations used were 0·02M-aniline and 0·01M-benzoyl chloride (dilution II). For certain compounds for which the reactions were too fast to be measured accurately at dilutions I and II, the concentrations used were 0·005M-aniline and 0·0025M-benzoyl chloride. Stubbs [1] showed that the velocity constant does not change appreciably with the dilution.

For the determination of the activation energy, E, velocity constants, k, in nitrobenzene and phenyl cyanide were measured at four or five different temperatures from 6° to 30°. For chlorobenzene, toluene, and bromobenzene velocity constants were determined at four different temperatures between 20° and 50°. Thermostats could be regulated to $\pm 0{\cdot}02°$ between 20° and 50°, and below 20° to $\pm 0{\cdot}05°$.

All materials were purified to constant m. p. or b. p. by recrystallisation or fractionation. " AnalaR " nitrobenzene was used as solvent.

The velocity constants were calculated from the equation

$$k = \frac{1}{120t}\left(\frac{1}{100 - x} - \frac{1}{100}\right) \times \frac{100}{a}$$

where k is the velocity constant in l. mole^{-1} sec.$^{-1}$, t the time in minutes, a the initial concentration of benzoyl chloride and x the percentage change. The experimental error in the velocity constants was about $\pm 2{\cdot}5\%$.

The results are summarised in Tables 1—4.

Discussion

From the results given in Table 1, $\log_{10} k_{25}$ has been plotted against the energy of activation E (Fig. 1). Out of eighteen compounds studied the results for more than half

[1] Stubbs, D.Phil. Thesis, Oxford University, 1948.

TABLE 1. *Parameters for the benzoylation of substituted anilines in nitrobenzene.*

Aniline	$100k_{25}$	$\log_{10} A$	E (cal./mole)	Diln.	Aniline	$100k_{25}$	$\log_{10} A$	E (cal./mole)	Diln.
m-Chloro-	12·9	3·34	5700	I	4-Chloro-2-methyl-	23·1	3·57	5700	I
p-Chloro-	40·4	3·29	5000	I	2 : 4-Dichloro-	0·287	3·70	8400	I
o-Chloro-	1·163	4·22	8400	I	2 : 5-Dichloro-	0·075	3·82	9400	I
m-Nitro-	1·685	3·54	7200	I	5-Bromo-2-methoxy-	8·20	3·60	6400	I
p-Nitro-	0·0766	3·56	9100	II	2-Methoxy-5-nitro-	1·755	4·31	8200	I
m-Bromo-	21·1	3·78	6000	I	2-Methyl-5-nitro-	0·551	4·56	9100	I
5-Chloro-2-methoxy-	11·04	3·53	6100	II	4-Chloro-3-nitro-	0·966	4·78	9200	I
5-Chloro-2-methyl-	7·14	4·09	7200	II	2-Methoxy-4-nitro-	0·598	3·02	8500	II
3-Chloro-2-methyl-	7·30	3·72	6600	I	2-Methyl-4-nitro-	0·0294	3·17	9100	II

TABLE 2. *Substituent effects calculated from the theoretical value of the activation energy of aniline in the solvent nitrobenzene.*

Substituent group	*m*-Chloro-	*p*-Chloro-	*o*-Chloro-	*m*-Nitro-	*p*-Nitro-	*m*-Bromo-	*o*-Methyl- *
ΔE (cal. mole^{-1}) ...	+1700	+1000	+4400	+3200	+5100	+2000	+500

* Calculated from the theoretical value of *o*-methylaniline.

TABLE 3. *Theoretical values for the activation energies of disubstituted anilines calculated additively.*

Aniline	E (calc.)	E (obs.)	Difference	Aniline	E (calc.)	E (obs.)	Difference
2 : 4-Dichloro-	9400	8400	+1000	3-Chloro-2-methyl-	6200	6600	−400
2 : 5-Dichloro-	12,800	9400	+3400	2-Methyl-4-nitro-	9600	9100	+500
4-Chloro-3-nitro- ...	8200	9200	−1000	4-Chloro-2-methyl-	5500	5700	−200
5-Chloro-2-methyl-	8900	7200	+1700				

TABLE 4. *Velocity constants at 25° ($100k_{25}$) in phenyl cyanide, chlorobenzene, bromobenzene, and toluene (dilution I).*

Aniline	Toluene	Chloro-benzene	Bromo-benzene	Phenyl cyanide	Aniline	Toluene	Chloro-benzene	Bromo-benzene	Phenyl cyanide
m-Chloro- ...	0·554	0·512	0·805	16·40	*m*-Nitro-	0·150	0·1116	0·1424	4·85
m-Methyl- ...	8·78	10·45	11·22	—	*p*-Chloro- ...	1·457	1·360	1·451	40·6
o-Methyl- ...	1·44	1·098	1·29	—	Aniline	5·55	5·99	7·22	—
p-Methyl- ...	20·75	23·60	31·65	—					

fall on or very near the line of slope $-2{\cdot}303RT$. Six compounds, namely 2-methoxy-5-nitro-, 4-chloro-3-nitro-, 2-methyl-5-nitro-, 5-chloro-2-methyl-, 2-methoxy-4-nitro-, and *o*-chloro-aniline, which are mainly substituted nitro-compounds, are further from the line than experimental error would account for. With them, not only the energy of activation but also the frequency factor varies.

Comparison of the Frequency Factor and the Energy of Activation in Benzene and Nitrobenzene.—When the medium is changed from benzene to nitrobenzene there is a general tendency for both the frequency factor and the activation energy to be decreased together, these effects influencing the rate in opposite senses. The net effect, however, is that the rate is several times greater in nitrobenzene. 2-Methyl-5-nitroaniline and 4-chloro-3-nitroaniline are exceptional in that the frequency factors are slightly higher than in benzene, but the energies of activation are lower as in all the other cases.

The frequency factor in the Arrhenius equation, for reactions in the liquid phase, can be considered in terms of the probability factor P and the number of collisions Z, or in terms of the factor $\alpha_A\alpha_B/\alpha^*$ where α_A and α_B are the activity coefficients of the two reactants A and B respectively and α^* is that of the so-called " activated complex."

According to the collision theory, Z decreases with the molecular weight of a reactant and increases with its diameter. In benzene solutions the molecular weight of benzoyl chloride is constant and the other factors do not vary much from compound to compound, so that Z is nearly constant. But for reactions in polar nitrobenzene it is not certain

whether the simple molecular weight of the reactants can be taken since molecules of the reactants may be more or less permanently loaded with molecules of the solvent which would increase the molecular weight from the point of view of collisions and hence effectively decrease Z. This factor might contribute to the lowering of the frequency factor but the influence is unpredictable and probably small.

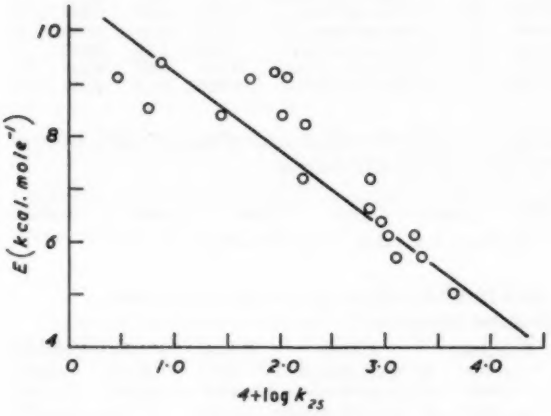

FIG. 1. *Plot of experimentally-measured activation energy against* log k_{25}.

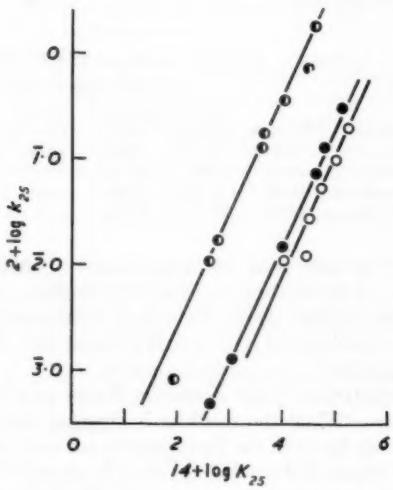

FIG. 2. *Plot of* log k_{25} *against logarithm of dissociation constant.*

◐ Nitrobenzene.
● Benzene.
○ Chlorobenzene.

According to the theory of reaction rates developed by Wynne-Jones and Eyring [3] and Stearn and Eyring [4]

$$A = (kT/h)(f_V^5/f_R^3 f_T^3)$$

where f_V, f_T, and f_R are partition functions for the vibrational, translational, and rotational degrees of freedom. The power indicates a product of that number of factors of the same type not necessarily equal. In benzoylation the product, and hence probably the activated complex, is more polar than the reactants. Solvation by the highly polar

[3] Wynne-Jones and Eyring, *J. Chem. Phys.*, 1953, **21**, 166.
[4] Stearn and Eyring, *J. Chem. Phys.*, 1937, **5**, 113.

nitrobenzene will therefore lower the activation energy from its value in a less polar solvent such as benzene. K will be governed by the equation

$$\text{Complex} + n \text{ solvent molecules} \rightleftharpoons \text{solvated complex}$$

The equilibrium constant will contain a term:

$$(\text{Partition function of complex})/(\text{Partition fuction of free solvent molecules})^n$$

The denominator will contain products of the form $(f_R^3 f_T^3)^n$ which will have been replaced in the numerator by f_V terms in corresponding numbers. Since $f_V \ll f_R$ or f_T, the result is a marked lowering of the frequency factor.

Thus the release of the energy of solvation, which lowers E, and the lowered frequency factor tend to compensate one another as the experimental findings show.

Relation between Velocity Constants and Dissociation Constants of the Amines.—If log k for the benzoylation of different substituted anilines in various solvents is plotted against the logarithm of the corresponding dissociation constant (in water), K, parallel straight lines are obtained (Fig. 2). The correlation can be explained on the basis of the dependence of both the basic strength and the rate of benzoylation on the availability of the unshared pair of electrons on the nitrogen atom.

It is noteworthy that the slopes of the lines are the same for two solvents of such widely different polarities as benzene and nitrobenzene. This shows that the solvent dipole does not interact with that due to the substituent in such a way as to alter the effect which the substituent can transmit to the reaction centre.

Additive Effects of the Substituents.—The energy of activation for the benzoylation of aniline in nitrobenzene could not be determined experimentally, since the reaction is too fast. It was therefore estimated by the following method. Since the plot of $\log_{10} k_{25}$ against $\log_{10} K$ is straight, and since the experimental point for aniline falls on the line in the case of benzene and chlorobenzene solutions, it is assumed that in the corresponding plot for nitrobenzene the point relating to aniline would again fall on the line. In this way the value of $\log_{10} k_{25}$ in nitrobenzene was estimated. The corresponding value of the energy of activation in nitrobenzene can be obtained from the plot of E against $\log_{10} k_{25}$. The estimated value of E is 4000 cal. mole^{-1}.

Table 2 contains the value of ΔE, the difference between E for the compound and E for aniline, in nitrobenzene. There is very little difference between the ΔE values for different groups in nitrobenzene and benzene, which again confirms the conclusion that for mono-substituted anilines the solvent does not alter the transmission of the electronic effects to the nitrogen atom.

Theoretical values for the activation energies of disubstituted anilines have been calculated by the addition of the values of ΔE for the two substituted groups to the value of E for aniline. Results in Table 3 show that for 3-chloro-2-methyl-, 4-chloro-2-methyl-, and 2-methyl-4-nitro-aniline the predicted and the experimental value of E agree well. For the rest of the compounds the difference is between 10% and 25%.

Other Solvent Effects.—The velocity constants k_{25} for the reaction in toluene, chlorobenzene, and bromobenzene (Table 4) are not very different from those for benzene and are much lower than the values for nitrobenzene and phenyl cyanide. This is qualitatively related to the last two solvents' having the highest dielectric constants, which results in solvation and lowered energy of activation. No relationship, however, could be obtained between the dipole moment of the various solvents and the velocity constants.

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823. *The Pigmentation and Cell-wall Material of* Daldinia *Sp.*

By D. C. Allport and J. D. Bu'Lock.

The chromogen of *D. concentrica* sporophores is 4 : 5 : 4′ : 5′-tetrahydroxydinaphthyl, which is oxidised enzymically to 4 : 9-dihydroxyperylene-3 : 10-quinone and to polymer. In the sporophores these oxidation products cross-link the cell-wall material, apparently by combining with non-acetylated amino-groups.

The fungus *Daldinia concentrica* (Bolt.) Ces. and de Not. is one of the larger Ascomycetes, occurring commonly in Britain as a parasite upon ash (*Fraxinus excelsior* L.) in which it causes a " white rot " with black staining and the condition known as " calico wood." At maturity it produces numerous fruit-bodies in the form of black hemisperical lumps up to 10 cm. across and with a characteristic zoned appearance in section. These eventually become light in weight and brittle, but younger specimens are denser and tougher and exude a little milky fluid on fracture; though ethanol extracts of such fruits are not deeply coloured they have a distinctive ultraviolet absorption spectrum and deposit a copious black precipitate on storage. This behaviour was under investigation when Anderson and Murray [1] reported the isolation of 4 : 9-dihydroxyperylene-3 : 10-quinone (I) from the sporophores; since this quinone [2] is almost black and virtually insoluble in most solvents it seemed possible that our own extracts might contain a more soluble precursor responsible for the characteristic absorption spectrum.

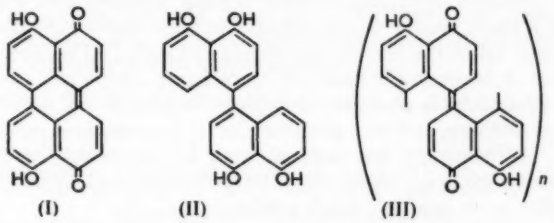
When a batch of sporophores had been broken up and defatted by extraction with light petroleum, ether-extraction afforded a solution ($\lambda_{max.}$ 313, 325, 340 mμ) from which the suspected precursor could be extracted by aqueous sodium carbonate (causing a bathochromic shift of 10—15 mμ) though not by sodium hydrogen carbonate solution. The solution gave an intense grey-green colour with ferric chloride, followed by a black precipitate. By chromatography on " Florisil " in chloroform, with careful exclusion of light and air from the column, a phenol was isolated as light brown crystals, m. p. 225—230° (decomp.). As attempts at further purification led only to deterioration, the compound was acetylated; this gave a stable derivative, m. p. 245°, for which elementary analysis and molecular-weight determination indicated a formula $C_{20}H_{10}(OAc)_4$.

The ultraviolet absorption spectrum of the phenol (cf. Table 1) is characteristic of naphthalene derivatives containing auxochromic substituents only in the α-positions.[3] Now, of the hydroxynaphthalenes of this type, those with two hydroxyl groups absorb at shorter wavelengths whilst 1 : 4 : 5-trihydroxynaphthalene absorbs at longer wavelengths. Since the close relation of the phenol to the perylene derivative (I) (see below) rendered unlikely the presence of substituents other than hydroxyl groups, a symmetrically hydroxylated 1 : 1′-dinaphthyl structure could be deduced from the spectroscopic data. The infrared absorption spectrum of the phenol was very similar to that of 1 : 8-dihydroxynaphthalene, and the presence of hydroxyl groups in *peri*-positions was confirmed by the effect of the phenol in depressing the pH of boric acid solution (see Table 2), the magnitude of the effect being characteristic.[4] This experiment failed to reveal the presence of other ionisable groups.

The instability of the phenol, with ready conversion into black pigments, has already been remarked upon, and the quinone (I) was identified amongst the oxidation products obtained under a variety of conditions. Thus the product from oxidation with chloranil in phenetole was partly soluble in tetrachloroethane or concentrated sulphuric acid, giving solutions with absorption spectra attributable [2] to the quinone (I) and on vacuum-sublimation afforded crystalline quinone (I), identified by its infrared absorption spectrum.[2]

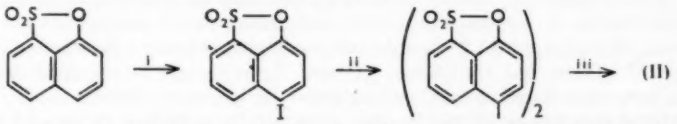
[1] Anderson and Murray, *Chem. and Ind.*, 1956, 376.
[2] Calderbank, Johnson, and Todd, *J.*, 1954, 1285.
[3] Daglish, *J. Amer. Chem. Soc.*, 1950, **72**, 4859.
[4] Hochstein, Stephens, Conover, Regna, Pasternack, and Woodward, *ibid.*, 1953, **75**, 5458.

Similarly the phenol gave a fairly stable pale yellow solution in concentrated sulphuric acid, from which deeply coloured solutions with the absorption spectrum of the quinone (I) were obtained on warming or on addition of nitric acid. The autoxidation of the phenol in dilute aqueous solutions was accelerated not only by alkali but also, more significantly, by the addition of crude mushroom phenolase or of an aqueous extract of *D. concentrica* mycelium; in each case the precipitated product was partly insoluble in concentrated sulphuric acid, and apparently polymeric, and partly soluble, giving a solution with the light absorption of the quinone (I).



(I) (II) (III)

These properties of the phenol suggested its formulation as 4 : 5 : 4′ : 5′-tetrahydroxy-1 : 1′-dinaphthyl (II). Attempts to isolate this compound from the products of the direct oxidative coupling of 1 : 8-dihydroxynaphthalene were unsuccessful, and it was therefore synthesised from 1 : 8-naphthasultone by the route shown. The acetates of the natural and synthetic products were identical in all respects.



Reagents: i, I + HNO_3 in AcOH–H_2SO_4. ii, Activated Cu bronze. iii, KOH fusion.

Oxidation of the tetrahydroxydinaphthyl (II) involves oxidative coupling of a type frequent in Nature,[5] a close analogy being the cyclisation of protohypericin.[6] The primary oxidation product can give rise either to the quinone (I) by internal coupling or to polymers such as (III) by intermolecular reaction. Such polymers, even at a low degree of polymerisation, would be black and highly insoluble. The primary oxidation product might be an extended dinaphthaquinone or a related semiquinonoid free radical; in this connection the very ready oxidative polymerisation of 1 : 8-dihydroxynaphthalene, which cannot form a quinone directly, should be noted.

Since the dinaphthyl (II) is so readily converted into the perylenequinone (I), the question of the occurrence of pre-formed quinone (I) in the sporophores seemed to merit further study. This quinone is virtually insoluble in acetone, yet Anderson and Murray record [1] that on continuous extraction of the sporophores with acetone a black precipitate, affording the quinone (I) on vacuum-sublimation, was deposited from the boiling solvent. They considered that the quinone had been solubilised by other constituents of the extracts. We were able to confirm that limited amounts of the quinone (I) do in fact occur in a free or loosely bound form in the sporophores. Thus cold concentrated sulphuric acid, which as noted above does not oxidise the dinaphthyl (II), extracts material with the absorption spectrum of the quinone (I). Moreover, after powdered sporophores have been exhaustively extracted with light petroleum and ether, further extraction with acetone affords, not only the black precipitate described by Anderson and Murray, but also a reddish-brown solution. This has an absorption spectrum similar to that of the quinone (I) in tetrachloroethane, but shifted some 10 mμ to shorter wavelengths. Warming

[5] Cf. Mason, *Adv. Enzymology*, 1955, **16**, 105, for general discussion.
[6] Brockmann, *Proc. Chem. Soc.*, 1957, 304.

this solution with dilute acid affords a precipitate from which the quinone (I) can be extracted by concentrated sulphuric acid or tetrachloroethane. This apparent solubilisation of the quinone (I) may be effected by some of the more polar constituents of the acetone extract (mannitol, sugars, etc.), either by association or by the formation of easily hydrolysed derivatives.

Presumably the perylenequinone (I) is formed from the dinaphthyl (II) in the fungus by an enzymic oxidation similar to that demonstrable *in vitro*; however, the amount of free or loosely bound quinone in the sporophores is insufficient to account for their intense blackness. After exhaustive extraction with organic solvents and water, the ground sporophores leave a black residue which retains the microscopic structure of the original material and is made up of the heavily pigmented cell-walls. This powder behaves as a quinonoid polymer; it is reversibly bleached by reducing agents and even in the reduced form contains no alkali-soluble phenols. A typical fungal cell-wall material is chitinous,[7] with up to 6·9% of nitrogen, and an equivalent acetyl content, in a poly-(*N*-acetylglucosamine) structure. By contrast, the material from *D. concentrica* contains only 2% of nitrogen and no acetyl groups. Moreover, after prolonged acid hydrolysis, over 30% of the material remains as an insoluble black powder.

These properties are explained if we suppose that the cell-wall polysaccharides contain non-acetylated amino-sugar residues and that in the sporophores these have been cross-linked by combination with monomeric or polymeric quinonoid oxidation products formed by enzymic oxidation of the dinaphthyl (II). The quinone (I) is known to react readily with amines,[2] and the formation of " melanochitin " by such a reaction presents some analogies to the process of " quinone tanning " of cuticular proteins in insects, etc.[8]

The isolation of a 1 : 1′-dinaphthyl derivative from natural sources has not previously been recorded, though some 2 : 2′-dinaphthyls are known as plant products, *e.g.*, diospyrol [9] and gossypol.[10] These, like the phenol (II) and the naturally occurring dianthryl derivatives, have structures based on identical moieties. In this they resemble the erythroaphins, in which the chromophore of the perylenequinone (I) was first detected,[2] though the relation of these compounds to the parent aphis pigments remains uncertain. Recently [11] the same chromophore has been detected in the pigment of various phytopathogenic fungi of a genus, *Elsinöe*, not unrelated to *Daldinia*. The genus *Daldinia* itself comprises a number of species closely similar to *D. concentrica*, and it is probable that the pigmentation of these is essentially similar to that described here. A preliminary communication of this work has already been published; [12] further work includes studies of *D. concentrica* in laboratory cultures.

Experimental

Extraction of D. concentrica *Sporophores.*—The sporophores, collected as available and stored in the dark at −5°, were minced and the coarse powder (875 g.) was steeped overnight in light petroleum, which was then filtered and the solid was continuously extracted with ether (2 l.) for 24 hr.; the ether was then renewed, and after a further 24 hr. a third portion of ether was employed to remove final traces of soluble material. The extracts were stored in the dark at −5° until required. In a typical procedure 350 ml. of the first ether extract (a red solution) were shaken with two portions of aqueous sodium carbonate (100, 50 ml.), and the aqueous extracts were combined and acidified with dilute hydrochloric acid. The solution and the tarry precipitated solids were extracted twice with fresh chloroform (containing 1% of ethanol) (100, 50 ml.), and the combined extracts were concentrated under reduced pressure to *ca.* 50 ml. This solution was put on a column (25 × 3 cm.) made up from a slurry of " Florisil "

[7] Tracey, in Paech and Tracey, " Modern Methods of Plant Analysis," Springer-Verlag, Berlin, 1955, Vol. II, p. 264.
[8] Reviewed by Dennel, *Biol. Rev.*, 1958, **33**, 178.
[9] Loder and Robertson, *J.*, 1957, 2233.
[10] Adams, Morris, Geissman, Butterbaugh, and Kirkpatrick, *J. Amer. Chem. Soc.*, 1938, **60**, 2193.
[11] Weiss, Flon, and Burger, *Arch. Biochem. Biophys.*, 1957, **69**, 311.
[12] Allport and Bu'Lock, *Proc. Chem. Soc.*, 1957, 264.

(Floridin Co., U.S.A.) in chloroform which had been boiled and stirred for 30 min. to expel air; the column was wrapped in black paper. Failure to exclude light and air led to deposition of insoluble purple pigment on the adsorbent. The column was eluted with chloroform, and the fractions giving a positive ferric chloride reaction were combined and evaporated under reduced pressure. The brown, partly solid residue was dissolved in ethanol (100 ml.), water (100 ml.) added, and the solution washed with light petroleum (2 × 50 ml.) to remove lipids. Most of the ethanol was then distilled off and the aqueous residue extracted with ether (3 × 50 ml.). The ether extracts were dried and evaporated, to give 4 : 5 : 4′ : 5′-tetrahydroxy-1 : 1′-dinaphthyl (II) as pale yellow crystals (0·3 g.) [ultraviolet spectrum, Table 1; infrared maxima (Nujol mull) at 760, 820, 896, 1040, 1140, 1320, 1395, 1530, 1590, 1608, 1631, and 3200 cm.$^{-1}$]. By spectroscopic assay, the content of dinaphthyl (II) in the initial ether extracts was found to be *ca.* 1% of the weight of sporophores.

TABLE 1. *Ultraviolet absorption spectra* ($\lambda_{max.}$ *in* mμ).

Compound	In EtOH	In alkali
1 : 8-Dihydroxynaphthalene	305, 320, 333	(317), 329, 342
4 : 5 : 4′ : 5′-Tetrahydroxy-1 : 1′-dinaphthyl (II)	313, 325, 340	(340) 350
1 : 4 : 5-Trihydroxynaphthalene	316, 333, 348	(310) 350

Values in parentheses denote inflexions.

Acetylation of the Dinaphthyl (II).—The phenol (II) (20 mg.) was heated under reflux in a nitrogen atmosphere with purified pyridine (1 ml.) and redistilled acetic anhydride (2 ml.); after 1 hr. water was added and the mixture repeatedly extracted with ether. The combined extracts were washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and evaporated, giving a yellow solid (25 mg.), which was purified by chromatography on deactivated alumina in acetone, treated with charcoal, and recrystallised from ethyl acetate to give 4 : 5 : 4′ : 5′-*tetra-acetoxy*-1 : 1′-*dinaphthyl*, m. p. 245° [Found: C, 69·15; H, 4·75%; *M* (Barger's method of isothermal distillation in acetone), 495 ± 15. $C_{28}H_{22}O_8$ requires C, 69·13; H, 4·56%; *M*, 486].

Borate Complexes.[4]—A Cambridge pH meter and calomel electrode were used to measure the pH difference between a solution containing 5 ml. of 0·5M-boric acid and 2 ml. of ethanol, and a solution containing 5 ml. of 0·5M-boric acid and the indicated quantity of the compound investigated dissolved in 2 ml. of ethanol. The results are shown in Table 2.

TABLE 2.

Compound	pH difference
(II) (10^{-3} mole)	3·9
1 : 8-Dihydroxynaphthalene (2×10^{-3} mole)	4·0
Catechol (2×10^{-3} mole)	1·3

4 : 9-*Dihydroxyperylene*-3 : 10-*quinone* (I).—The crude phenol (II) (240 mg. from 100 ml. of ether extract) was heated under reflux with chloranil (400 mg.) in phenetole (100 ml.); after 2½ hr. the solution was cooled and decanted into an excess of light petroleum; the black precipitate was washed with ethanol and benzene, dried, and sublimed at 260—300°/10^{-5} mm. to give dark red crystals of the quinone (I) (ultraviolet and infrared spectra as recorded by Calderbank *et al.*[2]).

Synthesis of the Phenol (II).—Glacial acetic acid (5 ml.), concentrated sulphuric acid (1·5 ml.), iodine (1·6 g.), and recrystallised 1 : 8-naphthasultone (2·0 g.; m. p. 156—157·5°) were stirred together whilst concentrated nitric acid (0·4 ml.) was added dropwise; the mixture was then heated at 70° for 45 min. until the iodine colour became permanent. The mixture was poured into water and the solid precipitate washed with aqueous sodium hydrogen sulphite and water, and recrystallised from acetic acid and benzene, affording 4-*iodo*-1 : 8-*naphthasultone* (2·6 g.), m. p. 205·5—206·5° (Found: C, 36·4; H, 1·6; I, 37·8. $C_{10}H_5O_3IS$ requires C, 36·05; H, 1·8; I, 38·15%). This product (0·8 g.) was heated in an oil-bath (220°) whilst activated copper bronze [13] (1·0 g.) was added during 45 min. with occasional stirring; heating was continued for a further 2 hr., and the mixture then cooled and extracted repeatedly with boiling benzene. The combined extracts were treated with charcoal and evaporated; the solid residue (0·24 g.) recrystallised from benzene to give 1 : 1′-*dinaphthyl*-4 : 5 : 4′ : 5′-*disultone*, m. p. 289—290° (Found: C, 58·9; H, 2·6. $C_{20}H_{10}O_6S_2$ requires C, 58·5; H, 2·5%). The disultone (0·2 g.),

[13] Kleiderer and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 4225.

mixed with potassium hydroxide (2·0 g.) and water (0·5 ml.), was heated under nitrogen to 240—280°, and, after frothing had subsided, to 310°; after 15 min. the black melt was cooled, dilute hydrochloric acid added, and the mixture extracted with ether, evaporation of which gave the crude dinaphthyl (II) with the correct ultraviolet absorption. The crude product was acetylated as described above, to give the tetra-acetyl derivative, m. p. and mixed m. p. 245°, the infrared spectrum of which, in Nujol mull, was identical with that of the naturally derived compound.

Attempted Oxidative Coupling of 1 : 8-*Dihydroxynaphthalene.*—1 : 8-Dihydroxynaphthalene was obtained from 1 : 8-naphthasultone by Erdmann's method;[14] in ethanol solution, it showed absorption max. at 333, 320, and 305 mμ. Addition of neutral aqueous potassium ferricyanide to the ethanol solution led to a green precipitate which was centrifuged and washed repeatedly with water. The solid residue, in ethanol solution, showed absorption max. attributable to the dinaphthyl (II), at 339, 324, and 311 mμ, but no useful yield of this compound could be obtained by this method.

Examination of Cell-wall Material.—The solid remaining after exhaustive ether-extraction of the sporophores was continuously extracted with acetone until no more material dissolved. The red acetone extract showed absorption max. at *ca.* 405 (infl.), 437, 470, (infl.), 520, and 560 mμ [in tetrachloroethane the quinone (II) shows max. at 419, 444, 493, 525, and 567 mμ], and when warmed with dilute hydrochloric acid deposited a black substance, partly soluble in concentrated sulphuric acid or tetrachloroethane to give solutions with the absorption spectra of the dinaphthyl (II). The black powder remaining after acetone-extraction was found, after drying, to contain 2·0% of nitrogen, and its acetyl content, determined by Scarisbrick's method for the acetyl content of chitinous substances,[7] was negligible; after the prolonged acid-hydrolysis in the acetyl determination, *ca.* 35% of the sample remained undissolved. When shaken with aqueous sodium dithionite the black powder assumed a light tan colour, rapidly becoming black on exposure to air.

We are grateful in Imperial Chemical Industries Limited, Dyestuffs Division, for materials, and to the University of Manchester for a research scholarship (to D. C. A.).

THE UNIVERSITY, MANCHESTER, 13. [*Received, June 16th,* 1958.]

[14] Erdmann, *Annalen*, 1888, **247**, 356.

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824. *The Preparation and Properties of Some* 2 : 3-*Benzo*-1 : 4-*diazepines.*

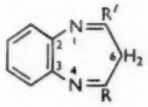
By I. L. FINAR.

1 : 6-Diphenylhexane-1 : 3 : 4 : 6- and octane-2 : 4 : 5 : 7-tetraone condense with one molecule of *o*-phenylenediamine to form 2 : 3-benzo-1 : 4-diazepines. The diazepine from the former with phenylhydrazine forms 1 : 3 : 1′ : 3′-tetraphenyl-5 : 5′-dipyrazolyl, whereas that from the latter gives a pyrazolyl-diazepine. Spectroscopic evidence is presented for the double bond structure of diazepine bases.

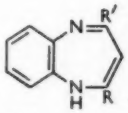
o-PHENYLENEDIAMINE with 1 : 2-diketones forms quinoxalines[1] and with 1 : 3-diketones forms 2 : 3-benzo-1 : 4-diazepines.[2] With triketones that are both 1 : 2- and 1 : 3-diketones quinoxalines have been obtained: pentane-2 : 3 : 4-trione forms 2-acetyl-3-methylquinoxaline,[3] and 1 : 4-diphenylbutane-1 : 2 : 4-trione forms 2-phenacyl-3-phenylquinoxaline.[4] In the present work, two tetraketones, 1 : 6-diphenylhexane-1 : 3 : 4 : 6- and octane-2 : 4 : 5 : 7-tetraone [5] (both are 1 : 2- and 1 : 3-diketones) have been condensed with one molecule of *o*-phenylenediamine, giving the diazepines (I) and (II), respectively.

[1] Hinsberg, *Annalen*, 1887, **237**, 327; von Pechmann, *Ber.*, 1888, **21**, 1411.
[2] Thiele and Steimmig, *Ber.*, 1907, **40**, 955.
[3] Sachs and Barschall, *Ber.*, 1901, **34**, 3047; Piutti, *Gazzetta*, 1936, **66**, 276.
[4] Lutz and Stuart, *J. Amer. Chem. Soc.*, 1936, **58**, 1885.
[5] Finar, *J.*, 1955, 1205.

Other possible products are the quinoxalines derived by condensation with the 1 : 2-diketone system present in the tetraketones. The infrared spectra of compounds (I) and (II), measured in Nujol suspension and in chloroform solution, are consistent with the diazepine structure since there is no absorption between 1680 and 1700 cm.$^{-1}$ for (I) (the phenacyl group is therefore absent) or between 1700 and 1720 cm.$^{-1}$ for (II) (the acetonyl group is therefore absent). There are, however, strong bands at 1590 cm.$^{-1}$ for (I) and at 1597 and 1567 cm.$^{-1}$ for (II), both consistent with the presence of an enolised 1 : 3-diketone group.



(A)



(B)

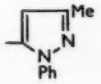
(I) ; R = CO·CH$_2$·COPh, R′ = Ph (VI); R =

(II) ; R = CO·CH$_2$·COMe, R′ = Me

(III); R = R′ = Me

(IV); R = Me, R′ = Ph

(V) ; R = R′ = Ph



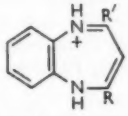
R′ = Me

Neither diazepine (I) nor (II) reacted with a second molecule of *o*-phenylenediamine.

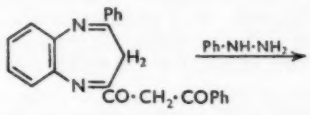
Diazepines have been comparatively little studied. Thiele and Steimmig [2] studied the benzodiazepines (III) and (IV) derived from acetylacetone and benzoylacetone and stated that an aqueous solution of the monohydrochloride of the former rapidly reacts with phenylhydrazine to form dimethylphenylpyrazole, and that of the latter to form methylphenylpyrazole. They also claim that both salts, when warmed in aqueous solution, readily decompose into benzimidazoles, and that dibenzoylmethane behaves like the other two diketones, but no details are given. Ried and Höhne [6] examined the conversion into imidazoles, and Lloyd and Marshall [7] investigated the bromination of 2 : 3-dihydro-1 : 4-diazepines.

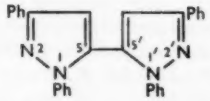
The conversion into pyrazoles has been repeated and extended to the diazepines (I) and (II); the hydrochloride of the dimethyl-compound (III) behaved as described, but that of the methylphenyl derivative (IV) liberated the free base. This, when refluxed with phenylhydrazine in acetic acid, gave 3-methyl-1 : 5-diphenylpyrazole,[8] which was also obtained similarly from the salt itself. The diphenyl-diazepine (V), prepared by warming dibenzoylmethane with *o*-phenylenediamine in ethanol–acetic acid, gave 1 : 3 : 5-triphenylpyrazole [9] when (V) was refluxed with phenylhydrazine in acetic acid.

The double-bond structure of the seven-membered ring is not certain. Thiele and Steimmig [2] suggested formula (A) or (B); Vaisman [10] suggested (C) for the monohydrochloride, and Lloyd and Marshall [11] believed (B) to be more likely than (A). The infrared spectrum of the diphenylbenzodiazepine (V) (dissolved in carbon tetrachloride) showed the presence of a methylene group (bands at 2901 and 2843 cm.$^{-1}$) and the absence of the NH stretching band. The diphenyl compound (V) appears to be of type (A).



(C)





When the phenacyl compound (I) was refluxed with phenylhydrazine in acetic acid 1 : 3 : 1′ : 3-tetraphenyl-5 : 5′-dipyrazolyl was obtained. This is the third isomer theoretically possible from the condensation between 1 : 6-diphenylhexane-1 : 3 : 4 : 6-tetraone

[6] Ried and Höhne, *Chem. Ber.*, 1954, **87**, 1801.
[7] Lloyd and Marshall, *J.*, 1958, 118.
[8] Knorr, *Ber.*, 1887, **20**, 1098; Drumm, *Proc. Roy. Irish Acad.*, 1931, **40**, *B*, 94.
[9] Knorr and Laubmann, *Ber.*, 1888, **21**, 1206.
[10] Vaisman, *Trudy Inst. Khim. Khar'kov Gosudarst. Univ.*, 1938, **4**, 157; 1940, **5**, 57 (*Chem. Abs.*, 1940, **34**, 5847; 1944, **38**, 750).
[11] Lloyd and Marshall, *J.*, 1956, 2597.

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and phenylhydrazine; the other two, 1 : 5 : 1′ : 5′-tetraphenyl-3 : 3′- and 1 : 5 : 1′ : 3′-tetraphenyl-3 : 5′-dipyrazolyl have already been isolated.[5]

The acetoacetyl compound (II) behaved differently under the same conditions; the product was a pyrazolyldiazepine, assumed to be (VI) by analogy with the reaction between benzoylacetone and phenylhydrazine.[5,12] The infrared spectrum of this pyrazolyldiazepine (in Nujol suspension) is consistent with the presence of an *o*-disubstituted aromatic ring; it includes a characteristic strong band at 752 cm.$^{-1}$ (which is absent from the spectrum of 5 : 5′-dipyrazolyl).

Experimental

5-Benzoylacetyl-7-phenyl-2 : 3-*benzo*-1 : 4-*diazepine* (I).—1 : 6-Diphenylhexane-1 : 3 : 4 : 6-tetraone [5] [in which paper, read 30 g. of acetophenone for 15 g.] (5·88 g., 0·02 mole) was added portionwise to *o*-phenylenediamine (2·16 g., 0·02 mole) in hot acetic acid (80 c.c.), and the mixture heated on the steam-bath for 15 min. The mixture was cooled and filtered, and the red precipitate washed with acetic acid and then with water, dried at 120°, and recrystallised from chloroform, giving the *benzodiazepine* (6·1 g., 83%) as red needles, m. p. 210° (Found: C, 79·1; H, 5·1; N, 7·55. $C_{34}H_{18}O_2N_2$ requires C, 78·7; H, 4·9; N, 7·65%).

An ethanolic solution of this diazepine did not give a coloration with ferric chloride. A solution in acetic acid was yellow, and addition of hydrochloric acid produced a deep red solution.

1 : 3 : 1′ : 3′-*Tetraphenyl*-5 : 5′-*dipyrazolyl*.—The benzodiazepine (I) (12·1 g., 0·033 mole), phenylhydrazine (10·8 g., 0·1 mole), and acetic acid (80 c.c.) were refluxed for 1 hr., and set aside overnight. The precipitate was washed with acetic acid and then with water, dried at 120°, and recrystallised from methanol, giving the *dipyrazolyl* (4·3 g., 30%) as white needles, m. p. 195—195·5° (Found: C, 81·9; H, 5·2; N, 12·6. $C_{30}H_{22}N_4$ requires C, 82·2; H, 5·0; N, 12·8%).

This dipyrazolyl gives a green colour in Knorr's pyrazoline test.

4 : 4′-*Dibromo*-1 : 3 : 1′ : 3′-*tetraphenyl*-5 : 5′-*dipyrazolyl*.—An acetic acid solution of the dipyrazolyl was treated with excess of bromine and heated on the steam-bath for 1 hr. The mixture was set aside overnight, and the precipitate was then collected and recrystallised from glacial acetic acid, giving the 4 : 4′-*dibromo-compound* as white rods, m. p. 175—176° (Found: Br, 26·8. $C_{30}H_{20}N_4Br_2$ requires Br, 26·8%).

5-*Acetoacetyl*-7-*methyl*-2 : 3-*benzo*-1 : 4-*diazepine* (II).—Octane-2 : 4 : 5 : 7-tetraone [5] (3·4 g., 0·02 mole) was added to *o*-phenylenediamine (2·16 g., 0·02 mole) in hot ethanol (30 c.c.), and the mixture heated (steam-bath) for 5 min. The mixture was cooled and filtered, and the orange precipitate recrystallised from ethanol, giving the *diazepine* (2·8 g., 58%) as orange needles, decomp. 186—188° (Found: C, 69·8; H, 5·8; N, 11·8. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8; N, 11·6%).

An ethanolic solution of this diazepine did not give an immediate colour with ferric chloride; the solution, however, slowly became red. The acetic acid solution was deep red, and the colour deepened on the addition of hydrochloric acid.

5-*Methyl*-7-(3-*methyl*-1-*phenyl*-5-*pyrazolyl*)-2 : 3-*benzo*-1 : 4-*diazepine* (VI).—The benzodiazepine (II) (2·42 g., 0·01 mole), phenylhydrazine (2·7 g., 0·025 mole), and acetic acid (30 c.c.) were refluxed for 1 hr. and then set aside overnight. The precipitate was collected, dissolved in hot acetic acid (charcoal), and filtered. The filtrate was cooled, diluted with water, and the precipitate recrystallised from methanol, giving the *pyrazolyldiazepine* (1·3 g., 41%) as yellow-orange leaflets, m. p. 166—167° (Found: C, 76·2; H, 5·68; N, 18·2. $C_{20}H_{18}N_4$ requires C, 76·4; H, 5·73; N, 17·8%).

A better yield was obtained when the two reagents were heated in a mixture of ethanol (30 c.c.) and acetic acid (10 c.c.) on the steam-bath for 1 hr. The mixture was cooled and the precipitate washed with ethanol (1·8 g., 57%).

An acetic acid solution of this diazepine was yellow, and the addition of hydrochloric acid produced a dark red colour.

3 : 5-*Dimethyl*-1-*phenylpyrazole*.—Phenylhydrazine (10·8 g., 0·1 mole) and a solution of 5 : 7-dimethyl-2 : 3-benzo-1 : 4-diazepinium chloride dihydrate [2] (9·78 g., 0·04 mole) in water (400 c.c.) were shaken vigorously. The mixture was extracted with ether, and the extract washed with aqueous sodium carbonate and then with water, dried (Na_2SO_4), and evaporated. The residual orange oil was distilled at 269—270° to give the dimethylphenylpyrazole as an

[12] Finar and Simmonds, *J.*, 1958, 200.

oil (5·6 g., 82%). This formed a picrate, m. p. and mixed m. p. with an authentic specimen 103—103·5° (McConnan [13] gives b. p. 270°, and m. p. of picrate 103°; von Auwers and Broche [14] give m. p. of picrate 100—101°).

3-Methyl-1 : 5-diphenylpyrazole.—Phenylhydrazine (8·64 g.; 0·08 mole), 5-methyl-7-phenyl-2 : 3-benzo-1 : 4-diazepinium chloride trihydrate [2] (13 g., 0·04 mole), and glacial acetic acid (150 c.c.) were refluxed for 1 hr. The solution was cooled and poured into a large excess of water, and the mixture extracted with ether. The ethereal solution was washed; the residue slowly solidified to the methyldiphenylpyrazole (6·4 g., 68·3%), m. p. 63°. This formed a picrate, m. p. and mixed m. p. with an authentic specimen 126—127° (Knorr [9] gives m. p. 63°; von Auwers and Stuhlmann [15] give m. p. of picrate 125—126°, and Drumm [8] gives m. p. 124°).

When an aqueous suspension of the diazepinium chloride trihydrate was shaken with an excess of phenylhydrazine, a yellow precipitate formed immediately. This, when refluxed with phenylhydrazine in acetic acid also gave the methyldiphenylpyrazole.

5 : 7-Diphenyl-2 : 3-benzo-1 : 4-diazepine (V).—Dibenzoylmethane (11·2 g., 0·05 mole) and *o*-phenylenediamine (5·4 g., 0·05 mole) in a mixture of ethanol (50 c.c.) and acetic acid (18 c.c.) were heated (steam-bath) for 3 hr. The mixture was cooled, and the precipitate recrystallised from ethanol, giving the *diazepine* (7·3 g., 49·3%) as fine white needles, m. p. 140—141° (Found: C, 84·8; H, 5·2; N, 9·8. $C_{21}H_{16}N_2$ requires C, 85·1; H, 5·4; N, 9·5%).

The solution of the diazepine in acetic acid or dilute hydrochloric acid was violet.

1 : 3 : 5-Triphenylpyrazole.—A mixture of the diazepine (V) (5·92 g., 0·02 mole) and phenylhydrazine (3·24 g., 0·03 mole) in acetic acid (30 c.c.) was refluxed for 1 hr., water (300 c.c.) added to the cooled solution, and the precipitate recrystallised from ethanol, giving the triphenylpyrazole (5·2 g., 87·8%), m. p. and mixed m. p. with authentic material 138° (Knorr and Laubmann [9] give m. p. 136·5—137·5°).

I thank Mr. H. Pyszora of the National College of Rubber Technology for the spectroscopic data.

THE NORTHERN POLYTECHNIC,
HOLLOWAY ROAD, LONDON, N.7.

[*Received, July 3rd*, 1958.]

[13] McConnan, *Ber.*, 1904, **37**, 3525.
[14] von Auwers and Broche, *Ber.*, 1922, **55**, 3910.
[15] von Auwers and Stuhlmann, *Ber.*, 1926, **59**, 1052.

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825. cis- *and* trans-3 : 4-cyclo*Pentanopiperidine.*

By G. G. AYERST and K. SCHOFIELD.

The compounds named above have been synthesised from *cis*- and *trans*-2-carboxy*cyclo*pentylacetic acid. The *cis*-base was identical with a compound previously obtained [1] by catalytic hydrogenation of 3 : 4-*cyclo*pentenopyridine. It provided an *N*-methyl derivative, which gave two isomeric *N*-oxides and a methiodide which underwent a normal Hofmann degradation. The *trans*-base was different from the product of sodium–ethanol reduction of 3 : 4-*cyclo*pentenopyridine, which has been shown to be unsaturated.

FOR a study of the possible influence of stereochemical factors on the pyrolysis of the *N*-oxides of cyclic tertiary bases, we needed the *cis*- (I; R = H) and the *trans*-isomer (II; R = H) of 3 : 4-*cyclo*pentanopiperidine, and of 3 : 4-*cyclo*heptanopiperidine, the lower and the higher homologue of decahydro*iso*quinoline. This paper describes some experiments in the first of these two series.

By catalytic hydrogenation of 3 : 4-*cyclo*pentenopyridine (III; R = H) Prelog and Metzler [1] obtained *cis*-3 : 4-*cyclo*pentanopiperidine. On the other hand, reduction with sodium and ethanol gave a base (picrate, m. p. 158°) which was taken to be the *trans*-isomer (II; R = H). Probably because of lack of material, physical constants for those bases were not given, and they were characterised only as picrates.

[1] Prelog and Metzler, *Helv. Chim. Acta*, 1946, **29**, 1170.

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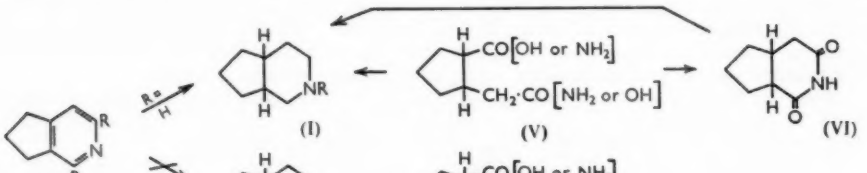
Prelog and Metzler [1] obtained 3 : 4-*cyclo*pentenopyridine (III; R = H) from the dihydroxy-compound (III; R = OH), through the dichloro-derivative. The dihydroxy-compound was prepared by cyclising ethyl α-cyano-α-(2-ethoxycarbonyl*cyclo*pent-1-enyl)-acetate (IV) with alkali, a method due to Kon and Nanji.[2] Re-examination of this route to the dihydroxy-compound (III; R = OH) proved it to be inconvenient. Like other



recent workers [3] we found the yield (53%) of ester (IV) obtainable from ethyl 2-oxo-*cyclo*pentanecarboxylate by Prelog and Metzler's method to be lower than that claimed, but a very minor modification greatly improved the process. The conditions described for the reaction by Kon and Nanji [2] were much less efficient, and an application of Cope's method [4] gave only 21% of ester (IV). However, the least satisfactory step in the sequence was the conversion (IV) ⟶ (III; R = OH). The yield of crude product was high, but of recrystallised material only 10—30%. Since the yield of the dichloro-compound (III; R = Cl) depended sharply on the purity of the dihydroxy-compound, considerable labour was needed to obtain any substantial quantity. Catalytic dechlorination proceeded smoothly. Reduction of the product (III; R = H) with sodium and alcohol gave what was clearly a mixture of bases. From this about 50% of a homogeneous picrate, m. p. 153—154°, was isolated, which seems to be the compound taken by Prelog and Metzler [1] to be the picrate of *trans*-3 : 4-*cyclo*pentanopiperidine.

For our purposes, routes to *cis*- and *trans*-3 : 4-*cyclo*pentanopiperidine more convenient than those described above were necessary. These seemed to be offered by the anhydrides of *cis*- and *trans*-2-carboxy*cyclo*pentylacetic acid, which were accordingly examined.

cis-2-Carboxy*cyclo*pentylacetic acid and its anhydride were readily obtained by the methods of Linstead and Meade [5] and Cook and Linstead.[6] The anhydride was converted by ammonia into a mixture of the ammonium salts of the amidic acids (V). Pyrolysis of the mixture gave a high yield of the crystalline *cis*-imide (VI), with a smaller amount of the diamide. In preparing the imide it was thus unnecessary to isolate the pure amidic acids. Work on these compounds will be described later. The imide (VI) was reduced smoothly by lithium aluminium hydride to give a moderately good yield of *cis*-3 : 4-*cyclo*pentanopiperidine (I; R = H), the picrate of which proved to be identical with the picrate of the base prepared by Prelog and Metzler's method. With formaldehyde–formic acid, *cis*-3 : 4-*cyclo*pentanopiperidine gave the tertiary base (I; R = Me) which was characterised as its picrate, methiodide, and methopicrate.

[2] Kon and Nanji, *J.*, 1932, 2426.
[3] Protiva, Mychajlyszyn, and Jflek, *Chem. Listy*, 1955, **49**, 1045.
[4] Cope, *J. Amer. Chem. Soc.*, 1941, **63**, 3452.
[5] Linstead and Meade, *J.*, 1934, 935.
[6] Cook and Linstead, *J.*, 1934, 956.

The crude mixture of amidic acids (V), obtained by acidifying the mixed ammonium salts described above, was also reduced with lithium aluminium hydride. The oily product consisted of a small yield of *cis*-3 : 4-*cyclo*pentanopiperidine and what was probably a mixture of amino-alcohols (VII). Examples of cyclisation of this kind occurring during reduction with lithium aluminium hydride have been encountered before,[7,8] notably by Segre and Viterbo [8] in the reduction of methyl β-(6-oxo-2-piperidyl)propionate and related compounds.

Efforts to apply a similar sequence of reactions to the preparation of *trans*-3 : 4-*cyclo*pentanopiperidine were only partly successful. *trans*-2-Carboxy*cyclo*pentylacetic acid and its anhydride were obtained by the methods of Cook and Linstead.[5] Comments on, and minor modifications to, these syntheses will be found below. All attempts to prepare the *trans*-imide have so far failed: heating the dicarboxylic acid with urea [9] gave only the diamide; treating the dicarboxylic anhydride with ammonia gave a mixture of ammonium salts of amidic acids, which on pyrolysis also produced the diamide; acidification of the mixed ammonium salts gave a mixture of the free amidic acids (to be described later). Like the mixture of *cis*-isomers, this mixture (VIII) was reduced with lithium aluminium hydride, giving some *trans*-3 : 4-*cyclo*pentanopiperidine (picrate, m. p. 144—145°) and a mixture of amino-alcohols. The latter could be converted into the cyclic base by treatment with hydrobromic acid followed by alkali, but conditions could not be found which made this cyclisation of practical value. *trans*-3 : 4-*cyclo*Pentanopiperidine (II; R = H) was converted into the *N*-methyl base (II; R = Me), characterised as its picrate and methiodide.

This preparation of *trans*-3 : 4-*cyclo*pentanopiperidine, though unsatisfactory as a source of the base in quantity, is unambiguous and raised the problem of the nature of the base (picrate, m. p. 158°) which Prelog and Metzler [1] regarded as the *trans*-saturated compound. The free base obtained from this picrate (our m. p. 153—154°) exhibited a higher refractive index than either *cis*- or *trans*-3 : 4-*cyclo*pentanopiperidine, and catalytic hydrogenation demonstrated the presence in it of one double bond. Furthermore, this saturation of the double bond produced *cis*-3 : 4-*cyclo*pentanopiperidine. Assuming that the double bond in the unsaturated base is in the heterocyclic ring, there are, of course, six possible structures for the compound. Four of these (two with the double bond terminating on nitrogen, and two with it situated αβ with respect to the –NH– group) seem to be eliminated by the observation that treatment of the unsaturated base with formaldehyde–formic acid gave an *N*-methylated base which was still unsaturated; with the double bond in the position mentioned, enamine reduction [10] to a saturated base would presumably have occurred. Of the two remaining structures (X; H for Me) seems to be rather more likely than (IX) both because of the resistance to reduction shown by the double bond and from the synthetic experiments described below.

With regard to the other product(s) of sodium–ethanol reduction of compound (III; R = H), the infrared spectrum of the crude reduction mixture strongly suggested the presence of *cis*-3 : 4-*cyclo*pentanopiperidine. In fact, it proved possible to isolate *cis*-*N*-methyl-3 : 4-*cyclo*pentanopiperidine when the crude base remaining after removal of the unsaturated component was methylated.

The work of Belleau [11] suggested an alternative approach to derivatives of 3 : 4-*cyclo*pentanopiperidine. The essential intermediate was *N*-methyl*cyclo*pent-1-enylacetamide (XI). The acetic acid is easily available (see p. 4103) and was readily converted through its acid chloride into the methylamide. This, with trioxymethylene in trifluoroacetic acid gave a mixture from which could be isolated what was probably reasonably pure lactam (XII) (not analysed). Reduction with lithium aluminium hydride gave a

[7] Barry, Belton, Kelly, and Twomey, *Nature*, 1950, **166**, 303.
[8] Segre and Viterbo, *Experientia*, 1958, **14**, 54.
[9] Ficken, France, and Linstead, *J.*, 1954, 3730.
[10] Leonard and Sauers, *J. Amer. Chem. Soc.*, 1957, **79**, 6210.
[11] Belleau, *Canad. J. Chem.*, 1957, **35**, 673.

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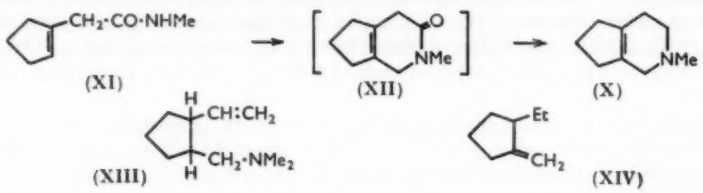
relatively unstable unsaturated base, of which the picrate (m. p. 155—157°) showed no mixed m. p. depression with the picrate (m. p. 150—151°) formed from the *N*-methylated



(XI) (XII) (X) (XIII) (XIV)

derivative of the unsaturated base resulting from sodium–ethanol reduction of **3 : 4-*cyclo*pentenopyridine**. The significance of the difference in m. p.s is uncertain, for when the unsaturated base from reduction of the lactam was treated with sodium in boiling ethanol, lithium–liquid ammonia, or sodium-*tert.*-butyl alcohol–liquid ammonia, it appeared to be unchanged, but the m. p. of its picrate could in no case then be raised above 151—152°. The unstable base from the lactam gave *N*-methyl-*cis*-**3 : 4-*cyclo*pentanopiperidine** on hydrogenation. This work does not fix unambiguously the position of the double bonds in the unsaturated derivatives, but seems to favour the inter-ring position.

cis-*N*-Methyl-**3 : 4-*cyclo*pentanopiperidine** readily gave a mixture of the two possible isomeric *N*-oxides (as picrates) when treated with hydrogen peroxide in methanol. We hope to study the pyrolysis of these isomers. Some of the expected products might be characterised by comparison with the products of the standard Hofmann degradation of *cis*-*N*-methyl-**3 : 4-*cyclo*pentanopiperidine** methiodide. This latter degradation proceeded normally,[12] giving at the first stage the methine (XIII). Hydrogenation, and continued Hofmann degradation to (XIV), followed by oxidation to 2-ethyl*cyclo*pentanone demonstrated the direction of the initial opening. Besides (XIV), the second step of the Hofmann degradation provided a base (characterised as its methiodide) which was apparently isomeric with *cis*-1-dimethylaminomethyl-2-ethyl*cyclo*pentane. It seems likely that this product was the *trans*-isomer of the latter.

Experimental

Ethyl α-Cyano-α-(2-ethoxycarbonylcyclopent-1-enyl)acetate.—(*a*) Ethyl 2-oxo*cyclo*pentanecarboxylate (20 g.), ethyl cyanoacetate (14·2 g.), ammonium acetate (2 g.), acetic acid (6 ml.), and benzene (25 ml.) were heated under reflux in a flask attached to a Dean and Stark water-separator, until no more water separated. The mixture was washed with water (3 × 40 ml.), and the aqueous layer was extracted with benzene. The benzene was removed under reduced pressure. Distillation of the residual oil gave ethyl α-cyano-α-(2-ethoxycarbonyl*cyclo*pent-1-enyl)acetate (6·9 g., 21·5%), b. p. 130—136°/0·05 mm.

(*b*) Ethyl 2-oxo*cyclo*pentanecarboxylate (20 g.), ethyl cyanoacetate (14 g.), and two drops of piperidine, allowed to react under the conditions of Kon and Nanji,[2] gave the same product (5·76 g., 20·8%), b. p. 117°/0·02 mm.

(*c*) Ethyl 2-oxo*cyclo*pentanecarboxylate (158·3 g.), ethyl cyanoacetate (115 g.), and piperidine (26·2 ml.) reacted under the conditions of Prelog and Metzler,[1] to give the product (126·8 g., 50%), b. p. 130—140°/0·05 mm.

A mixture of ethyl 2-oxo*cyclo*pentanecarboxylate (206·3 g.), ethyl cyanoacetate (151 g.), and piperidine (34·5 ml.) was set aside for 48 hr. Ether was added and the mixture was washed with dilute hydrochloric acid. Distillation of the dried ethereal layer gave the product (226 g., 68%), b. p. 130—136°/0·15 mm.

3 : 4-cyclo*Pentenopyridine* (III; R = H).—By the method of Prelog and Metzler [1] ethyl α-cyano-α-(2-ethoxycarbonyl*cyclo*pent-1-enyl)acetate gave 10—30% of pure **2 : 6-dihydroxy-3 : 4-*cyclo*pentenopyridine**. This gave the **2 : 6-dichloro-compound** in 76% yield, but use of the crude dihydroxy-compound gave only 14% of the dichloro-derivative. Dechlorination of **2 : 6-dichloro-3 : 4-*cyclo*pentenopyridine** gave **3 : 4-*cyclo*pentenopyridine** in 80% yield (as

[12] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell & Sons, London, 1953, p. 429.

picrate). Decomposition of the picrate (18·9 g.) with 10% sodium hydroxide solution (150 ml.), followed by steam-distillation and extraction of the distillate with ether, gave 3 : 4-*cyclo*pentenopyridine (5·6 g.), b. p. 78—80°/10 mm., n_D^{18} 1·5380.

Reduction of 3 : 4-cyclo*Pentenopyridine with Sodium and Ethanol.*—3 : 4-*cyclo*Pentenopyridine (4·05 g.) in boiling ethanol (300 ml.) was treated with sodium (25 g.) during 2 hr. The cooled mixture was acidified with concentrated hydrochloric acid. The residue left after removal of ethanol was basified with sodium hydroxide solution and extracted with ether. Distillation of the dried (K_2CO_3) extracts gave a mixture of bases (3·0 g.), b. p. 77—78°/16 mm., n_D^{18} 1·5000. This (2·5 g.) was treated with picric acid (4·5 g.) in ethanol. Fractional crystallisation of the product from ethanol gave yellow rhombs of a fairly insoluble picrate " A " (2·05 g.), m. p. 153—154° (Found: C, 47·8; H, 4·9. Calc. for $C_{14}H_{16}O_7N_4$: C, 47·7; H, 4·6%). From the mother-liquors an inseparable mixture of picrates " B " (1·94 g.) was recovered.

Picrate " A " (1·65 g.) was decomposed with sodium hydroxide solution, and the free base (0·43 g.; b. p. 72—73·5°/11 mm., n_D^{18} 1·5110) isolated in the usual way by steam-distillation and ether-extraction. The base (0·22 g.), 40% aqueous formaldehyde (0·4 ml.), and 98% formic acid (0·6 ml.) were heated for 4 hr. on the steam-bath. The solution was basified with potassium carbonate and extracted with ether. Treatment of the base recovered from the dried (K_2CO_3) extract with picric acid in ethanol gave a *picrate* which formed yellow needles, m. p. 150—151° (Found: C, 49·6; H, 5·5; N, 15·5. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 5·0; N, 15·3%), from the same solvent.

When the unsaturated base (0·169 g.) from picrate " A," reduced Adams's catalyst (0·1 g.), and ethanol (10 ml.) were shaken with hydrogen, uptake (29·6 ml.; theor., 30·9 ml.) was complete in 3 hr. Removal of the catalyst, concentration, treatment with picric acid, and recrystallisation from ethanol gave *cis*-3 : 4-*cyclo*pentanopiperidine (0·35 g.), m. p. and mixed m. p. with authentic material (see below), 138—140°.

The bases liberated in the same way from the mixture of picrates " B " (1·6 g.) were methylated similarly. The methylated product was converted into a mixture of picrates. Fractional crystallisation from ethanol gave, as the only homogeneous material which could be isolated, *cis*-1-methyl-3 : 4-*cyclo*pentanopiperidine picrate (0·6 g.) as long yellow needles, m. p. and mixed m. p. with authentic material, 210—211°. A mixture with *trans*-1-methyl-3 : 4-*cyclo*pentanopiperidine picrate (m. p. 213·5—214°) had m. p. 205—206°.

Imide (VI) *of* cis-2-*Carboxy*cyclo*pentylacetic Acid.*—*cis*-2-Carboxy*cyclo*pentylacetic anhydride [6] (85·3 g.) was heated under reflux with aqueous ammonia (1350 ml.; *d* 0·880) for 1 hr. Water was removed under reduced pressure and the residue was pyrolysed at 160° for 3 hr. The crystalline product was extracted with ether and recrystallised from ether–light petroleum (b. p. 60—80°). The *imide* formed platelets (70·8 g.), m. p. 89·5—91° (Found: C, 63·0; H, 7·2; N, 8·9. $C_8H_{11}O_2N$ requires C, 62·7; H, 7·2; N, 9·1%).

cis-3 : 4-cyclo*Pentanopiperidine* (I; R = H).—(i) The imide (59·4 g.) was extracted (Soxhlet) into a boiling mixture of ether (250 ml.) and lithium aluminium hydride (59 g.). Boiling was continued for 1 hr. after all the imide had been extracted. The mixture was decomposed with wet ether, and the product liberated by addition of solid sodium hydroxide. It was isolated by continuous extraction (24 hr.) with ether. Processing of the dry (Na_2SO_4) extract gave the base (23·2 g.), b. p. 71—73°/14 mm., n_D^{18} 1·4892 (Found: C, 76·7; H, 11·8; N, 11·4. Calc. for $C_8H_{15}N$: C, 76·7; H, 12·1; N, 11·2%). The picrate separated as pale yellow needles, m. p. 142—143° (Found: C, 47·8; H, 5·0. Calc. for $C_{14}H_{18}O_7N_4$: C, 47·5; H, 5·1%), which did not depress the m. p. of a specimen prepared by the method of Prelog and Metzler.[1]

(ii) *cis*-2-Carboxy*cyclo*pentylacetic anhydride (78 g.) in benzene (500 ml.) was treated with dry ammonia for 2 hr. The very deliquescent mixture of ammonium salts was collected and freed from solvent in a desiccator. The white powder was acidified with hydrochloric acid, and the resulting amidic acid extracted from ammonium chloride by boiling tetrahydrofuran in a Soxhlet apparatus. Removal of the tetrahydrofuran under reduced pressure left a sticky solid. A portion of this mixture (15 g.) was extracted (Soxhlet) into a boiling mixture of tetrahydrofuran (250 ml.) and lithium aluminium hydride (12 g.), and then boiled for 4 hr. The product, isolated in the usual way, gave on distillation *cis*-3 : 4-*cyclo*pentanopiperidine (1·53 g.), b. p. 76—80°/16 mm., n_D^{18} 1·4908 (identified as the picrate, m. p. 138—140°), and a heavy colourless oil, b. p. 152—160°/16 mm., $n_D^{16\cdot5}$ 1·4974. The latter was probably a mixture of amino-alcohols.

cis-1-*Methyl*-3 : 4-cyclo*pentanopiperidene* (I; R = Me).—*cis*-3 : 4-*cyclo*Pentanopiperidine

(23·2 g.), 40% formaldehyde (25 ml.), and 98% formic acid (36 ml.) were heated under reflux for 4 hr. The usual processing gave the 1-*methyl base* (22·88 g., 88·7%), b. p. 64—66°/12 mm., n_D^{19} 1·4745 (Found: C, 77·5; H, 12·4; N, 9·8. $C_9H_{17}N$ requires C, 77·6; H, 12·3; N, 10·0%). The *picrate* formed yellow needles, m. p. 210·5—211·5° (Found: C, 48·9; H, 5·2. $C_{15}H_{20}O_7N_4$ requires C, 48·9; H, 5·5%), from ethanol. The *methiodide* (44·76 g., 96·8%) was prepared by addition, with cooling, of methyl iodide (115 g.) to the *N*-methyl base (22·88 g.); it crystallised from ethanol in colourless needles, m. p. 254—255° (Found: C, 42·4; H, 6·9. $C_{10}H_{20}NI$ requires C, 42·7; H, 7·2%). The *methopicrate* prepared from the methiodide crystallised from ethanol as feathery yellow plates, m. p. 167·5—168·5° (Found: C, 50·4; H, 5·7. $C_{16}H_{22}O_7N_4$ requires C, 50·3; H, 5·8%).

cis-1-*Methyl*-3 : 4-cyclo*pentanopiperidine* 1-*Oxides*.—35% Hydrogen peroxide (1·5 ml.) was added slowly with stirring to ice-cold *cis*-1-methyl-3 : 4-*cyclo*pentanopiperidine (0·48 g.) in methanol (1 ml.). The mixture became homogeneous after 1 hr. and was left at room temperature for 24 hr. Platinum black prepared from Adams's catalyst (0·03 g.) in methanol (5 ml.) was added and the whole stirred for 1 hr. more. The catalyst was filtered off and the filtrate was treated with picric acid (0·83 g.) in boiling water (15 ml.). The immediate bright yellow precipitate (1·26 g.) was fractionally crystallised from ethanol to give two picrates. The more insoluble *picrate* crystallised as yellow needles, m. p. 185—186° (Found: C, 46·7; H, 5·7. $C_{15}H_{20}O_8N_4$ requires C, 46·9; H, 5·3%). The isomeric *picrate* crystallised as small pale yellow needles, m. p. 164—165° (Found: C, 47·2; H, 5·2%).

trans-2-*Carboxy*cyclo*pentylacetic Anhydride*.—*cyclo*Pentanone (100 g.), potassium cyanide (60·6 g.), and water (200 ml.) were stirred together below 10° and treated with 40% sulphuric acid (200 ml.) during 3 hr.[13] The mixture was stirred overnight at 0°. Distillation of the dried (Na_2SO_4) ether extract of the resulting oil gave *cyclo*pentanone cyanohydrin (90 g.), b. p. 118—119°/14 mm. This was converted into 1-cyano*cyclo*pentene. The nitrile (63·5 g.), ethanol (124 ml.), and concentrated sulphuric acid (78 ml.) were boiled for 48 hr. Processing gave ethyl *cyclo*pent-1-enecarboxylate (51·3 g.), b. p. 90—92°/23 mm., and a residue of *cyclo*pent-1-enecarboxyamide (17 g.), m. p. 205—210° (reported,[14] m. p. 210°). Addition of diethyl sodiomalonate to the ester under Cook and Linstead's [6] conditions gave only 40% of diethyl *trans*-2-ethoxycarbonyl*cyclo*pentylmalonate. Use of a half-molar excess of diethyl malonate raised the yield to 66%. The remaining steps to the anhydride went as reported.[6]

trans-2-*Carboxy*cyclo*pentylacetic Diamide*.—(i) The anhydride (1 g.) was heated under reflux for 1 hr. with aqueous ammonia (15 ml.; *d* 0·880). After evaporation to dryness under reduced pressure a residue remained which was pyrolysed at 120—160° for 3 hr. The resulting oil solidified when triturated with methanol, and crystallisation from this solvent gave needles of the *diamide*, m. p. 180—183° (Found: C, 56·3; H, 8·0. $C_8H_{14}O_2N_2$ requires C, 56·4; H, 8·3%).

(ii) The anhydride (1 g.) was heated for 1 hr. at 135° with urea (0·22 g.). After cooling, it was treated with methanol to give a product (0·6 g.) which after two recrystallisations from methanol had m. p. 178—180°.

trans-3 : 4-cyclo*Pentanopiperidine* (II; R = H).—*trans*-2-Carboxy*cyclo*pentylacetic anhydride (38·5 g.) in dry benzene (400 ml.) was treated with dry ammonia for 2 hr. Working up as before gave the mixed amidic acids (28·7 g.; m. p. 152—156°). This mixture (10 g.) was reduced as in the case of the mixed *cis*-acids with tetrahydrofuran (250 ml.) and lithium aluminium hydride (10·9 g.). Distillation of the product gave *trans*-3 : 4-*cyclo*pentanopiperidine (0·66 g.), b. p. 76—78°/20 mm., n_D^{19} 1·4830 [the *picrate* formed prisms, m. p. 144—145° (Found: C, 47·3; H, 5·1; N, 15·6. $C_{14}H_{18}O_7N_4$ requires C, 47·4; H, 5·1; N, 15·8%), from ethanol], and a mixture of amino-alcohols (5·43 g.), b. p. 130—132°/7 mm., n_D^{21} 1·4885 (Found: C, 67·3; H, 11·8. $C_8H_{17}ON$ requires C, 67·1; H, 11·9%).

The mixed amino-alcohols (1 g.) were heated under reflux with 50% hydrobromic acid (25 ml.) for 8 hr. The hydrobromic acid was removed under reduced pressure and the sticky residue was dissolved in water (50 ml.) and added slowly to 0·1N-sodium hydroxide (153 ml.). The mixture was kept at 45—50° for 3½ hr., then subjected to steam-distillation. From the distillate ether recovered a base (0·35 g.). Conversion into the picrate and recrystallisation from ethanol gave *trans*-3 : 4-*cyclo*pentanopiperidine picrate (0·4 g.), m. p. 143—144°. The use of 60% hydrobromic acid did not improve the cyclisation.

[13] *Org. Synth.*, Collected Vol. II, p. 7.
[14] Buu-Hoï and Cagniant, *Bull. Soc. chim. France*, 1945, **12**, 978.

trans-1-*Methyl*-3 : 4-cyclo*pentanopiperidine* (II; R = Me).—Methylation of the *trans*-base (0·2 g.) in the usual way, with 40% aqueous formaldehyde (0·3 ml.) and 98% formic acid (0·4 ml.), gave the 1-methyl base, the *picrate* of which formed yellow needles, m. p. 213·5—214° (Found: C, 48·3; H, 5·5. $C_{15}H_{20}O_7N_4$ requires C, 48·9; H, 5·5%), from ethanol. The *methiodide* separated from ethanol as needles, m. p. 219—220° (Found: C, 43·0; H, 7·3. $C_{10}H_{16}NI$ requires C, 42·7; H, 7·2%).

N-*Methyl*cyclo*pent*-1-*enylacetamide* (XI).—*cyclo*Pentanone (25 g.), ethyl cyanoacetate (42 g.), ammonium acetate (5·9 g.), and acetic acid (11·8 ml.) in dry benzene (250 ml.) gave, by the general procedure of Cope,[4] ethyl α-cyano-α-*cyclo*pent-1-enylacetate (51 g.), b. p. 156—158°/18 mm., m. p. 52—54°. Hydrolysis of the ester (10·3 g.) with boiling concentrated hydrochloric acid for 3½ hr., followed by concentration to 40 ml., gave the acid [6·5 g.; m. p. 126—128°, after crystallisation from ether–light petroleum (b. p. 60—80°)]. Pyrolysis of the acid (8·66 g.) at 210—230° for 10 min. and distillation of the residue gave *cyclo*pent-1-enylacetonitrile (4·76 g.), b. p. 80—82°/18 mm. The method of Sugasawa and Saito [15] was slightly more convenient, and gave 53·1 g. of the nitrile from 50 g. of *cyclo*pentanone. The nitrile (53·1 g.) was boiled overnight with aqueous potassium hydroxide (106 g. in 750 ml. of water). Acidification, ether-extraction, and distillation gave *cyclo*pent-1-enylacetic acid [16] (46 g.), b. p. 134—136°/18 mm.

Pure thionyl chloride (63 ml.) was added to a stirred solution of *cyclo*pent-1-enylacetic acid (52 g.) in dry benzene (170 ml.), and the solution was then heated under reflux for 1 hr. Benzene and excess of thionyl chloride were removed under reduced pressure, and the process was repeated three times with dry benzene (3 × 150 ml.). A solution of the residue in benzene (200 ml.) was stirred in an ice-bath and treated slowly with 25% aqueous methylamine (96 ml.) so that the temperature did not rise above 10°. After 1½ hr. the organic layer was separated, and the aqueous layer extracted with benzene (100 ml.). Distillation of the combined benzene solutions gave, after drying, N-*methyl*cyclo*pent*-1-*enylacetamide* (37 g.), b. p. 158—160°/20 mm., n_D^{17} 1·4945 (Found: C, 69·1; H, 9·2. $C_8H_{13}ON$ requires C, 69·0; H, 9·4%), which solidified (m. p. < 30°).

Tetrahydro-1-*methyl*-3 : 4-cyclo*pentenopyridine* (X).—The amide (37 g.), trifluoroacetic acid (116 g.), and trioxymethylene (9·6 g.) were heated on the water-bath for 6 hr. The solvent was removed under slightly reduced pressure, and the residue was then distilled. The product (33 g., b. p. 142—152°/10 mm.) was distilled through a column packed with helices, giving an oil (11·9 g.), b. p. 84—86°/1 mm., n_D^{21} 1·4730 (evidently the pyridone), and unchanged methylamide (16 g.; b. p. 158—164°/16 mm., n_D^{21} 1·4960).

The pyridone (15 g.) in dry ether (50 ml.) was added to lithium aluminium hydride (10·2 g.) in dry ether (75 ml.) fast enough to maintain boiling. After these had been heated for 3 hr. under reflux, working up by the usual methods gave the product (5·34 g.), b. p. 72—76°/18 mm., n_D^{17} 1·4840, which formed a *picrate*, m. p. 155—157° (Found: C, 48·7; H, 5·3. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 5·0%), as yellow needles from ethanol. Subsequent preparations of the picrate from the attempted reductions by dissolving metals gave homogeneous products, m. p. 151—153°, whose m. p.s could not be raised by further recrystallisation and which gave no depression with the above picrate (m. p. 155—157°). The *methiodide* crystallised from acetone–ether in needles, m. p. 146—147° (Found: C, 43·3; H, 6·7. $C_{10}H_{18}NI$ requires C, 43·0; H, 6·5%).

Hydrogenated in ethanol (5 ml.) in the way described above, the tetrahydropyridine (0·23 g.) took up 37·75 ml. of hydrogen (theor., 37·6 ml.) in 45 min. In the usual way the resulting solution provided *cis*-1-methyl-3 : 4-*cyclo*pentanopiperidine picrate (0·4 g.), m. p. and mixed m. p. 210·5—211°. A mixture with the *trans*-isomer (m. p. 213·5—214°) had m. p. 207—208°.

Hofmann Degradation of cis-1-*Methyl*-3 : 4-cyclo*pentanopiperidine Methiodide*.—The methiodide (4·2 g.) in water (60 ml.) was shaken in the dark with silver oxide (from 5·0 g. of silver nitrate) until an iodide test was negative. The filtered solution was evaporated under reduced pressure at 45—50°, and the temperature was then raised to 120—130°, providing a distillate of *cis*-1-dimethylaminomethyl-2-vinyl*cyclo*pentane, b. p. 65—70°/15 mm. This gave a *picrate* which crystallised from ethanol as yellow platelets, m. p. 123·5—124·5° (Found: C, 50·7; H, 5·7; N, 14·9. $C_{16}H_{22}O_7N_4$ requires C, 50·3; H, 5·8; N, 14·7%), and a *methiodide*, forming plates, m. p. 229—230° (Found: C, 45·2; H, 7·7. $C_{11}H_{22}NI$ requires C, 44·8; H, 7·5%), from acetone–ether.

The crude unsaturated base from the above decomposition was hydrogenated in ethanol

[15] Sugasawa and Saito, *Pharm. Bull.* (*Japan*), 1956, **4**, 237.
[16] Harding and Haworth, *J.*, 1910, 486.

with 30% palladised charcoal (0·2 g.), giving *cis*-1-dimethylaminomethyl-2-ethyl*cyclo*pentane (1·4 g.), b. p. 82—83°/22 mm., n_D^{16} 1·4540. The *picrate* formed yellow rhombs, m. p. 84—85° (Found: C, 49·8; H, 6·2. $C_{16}H_{24}O_7N_4$ requires C, 50·0; H, 6·3%), from ethanol. The *methiodide* gave platelets, m. p. 215—217° (Found: C, 44·7; H, 8·0. $C_{11}H_{24}NI$ requires C, 44·45; H, 8·1%), from acetone–ether. The oxide, prepared as described above, formed a yellow *picrate*, m. p. 104·5—106° (Found: C, 47·6; H, 5·8. $C_{16}H_{24}O_8N_4$ requires C, 48·0; H, 6·0%), which gave platelets from ethanol.

cis-1-Dimethylaminomethyl-2-ethyl*cyclo*pentane methiodide (9·53 g.) was submitted to Hofmann degradation as described above. The oily distillate was separated, after ether-extraction, by 2N-hydrochloric acid into a neutral (2·56 g.) and a small basic fraction. The basic fraction provided a *methiodide* which crystallised as platelets, m. p. 253—254° (Found: C, 44·7; H, 7·9. $C_{11}H_{24}NI$ requires C, 44·45; H, 8·1%), from acetone–ether.

The neutral product (0·43 g.) in dry ethyl acetate was treated with ozone for 8 hr. The solution was shaken with Adams's catalyst and hydrogen until reduction ceased, then filtered and distilled. The crude product (0·2 g., b. p. 160—200°) formed a semicarbazone which crystallised from aqueous alcohol in white plates, m. p. 179—180° (Found: C, 57·0; H, 9·1. Calc. for $C_8H_{15}ON_3$: C, 56·8; H, 8·95%), alone and mixed with 2-ethyl*cyclo*pentanone semicarbazone (m. p. 180—182°).

2-*Ethyl*cyclo*pentanone*.—Ethyl 1-ethyl-2-oxo*cyclo*pentane-1-carboxylate [17] (9·8 g.), acetic acid (50 ml.), 48% hydrobromic acid (50 ml.), and water (25 ml.) were heated under reflux for 18 hr. About half of the mixture was removed by distillation under reduced pressure. The distillate was basified with solid sodium hydroxide and extracted with ether. The washed (sodium hydrogen carbonate) and dried (Na_2SO_4) extract gave 2-ethyl*cyclo*pentanone (4·5 g.), b. p. 152—160° (semicarbazone, m. p. 180—182°).

We are grateful to D.S.I.R. for a maintenance grant (to G. G. A.), and to Professor Prelog who kindly presented us with a specimen of *cis*-3 : 4-*cyclo*pentanopiperidine picrate.

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PRINCE OF WALES ROAD, EXETER. [*Received, May 13th*, 1958.]

[17] Case and Reid, *J. Amer. Chem. Soc.*, 1928, **50**, 3064.

826. *The Synthesis of 4-Aminopteridines as Potential Anti-metabolites.*

By C. L. LEESE and G. M. TIMMIS.

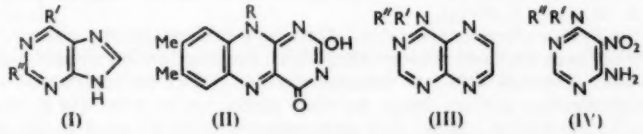
A number of pteridines which carry alkylamino- and dialkylamino-substituents in the 4-position have been synthesised.

RECENTLY it has been shown that in the conversion of adenine [1] (I; R′ = NH_2, R″ = H) and guanine [2] (I; R′ = OH, R″ = NH_2) to riboflavine by the organism *Eremothecium ashbyii* the pyrimidine ring is transferred from the purine to riboflavine (II; R = ribityl) practically intact. This process appears to involve essentially an opening of the glyoxaline ring of the purine with loss of $C_{(8)}$ and condensation of the diaminopyrimidine so formed, perhaps after glycosidation of one amino-group, with 3 : 4-dimethyl-*o*-benzoquinone.

The ability of purines to open up to yield diaminopyrimidines was first shown *in vitro* by Albert and when this was done in the presence of suitable diketones pteridines were formed.[3] The suggestion that this sequence might occur in Nature was later confirmed [4] and this process could be a source of pteridine vitamins and co-factors. The occurrence of the 4 : 5-dimethyl-1 : 2-phenylene grouping in both riboflavine and vitamin B_{12} suggests that these two vitamins may be biosynthetically interdependent and therefore that they would depend also on purine and pteridine metabolism. Since this overall relationship would involve a balance of the four components it is likely that, for example, interference

[1] McNutt, *J. Biol. Chem.*, 1956, **219**, 365.
[2] Usama and al-Khalidi, *Fed. Proc.*, 1958, **17**, 180.
[3] Albert, *Biochem. J.*, 1954, **57**, x.
[4] Albert, *ibid.*, 1957, **65**, 124.

with the function of the normal pteridines would have interesting biological effects and we have, therefore, synthesised some simple pteridines (III) as potential antimetabolites according to the concept of structural analogy. These pteridines were selected because they are formally derivable from 6-arylalkylaminopurines [5] and from the 6-dimethylaminopurine moiety of puromycin; both these structures are associated with growth inhibition in a variety of organisms.



(I) (II) (III) (IV)

The required intermediates (IV; R′ = H, R″ = phenethyl, furfuryl, benzyl, or *cyclo*hexyl and R′ = R″ = Me) were conveniently made by condensing 4-amino-6-chloro-5-nitropyrimidine with the appropriate amine in ether, reaction being smooth at room temperature and giving excellent yields. The nitropyrimidines were reduced with hydrogen and Raney nickel, and the triamines produced then yielded the pteridines on reaction with glyoxal.

Experimental

Analyses are by Mr. P. R. W. Baker, Beckenham.

4-Amino-6-(substituted amino)-5-nitropyrimidines.—These compounds were prepared by reaction of 4-amino-6-chloro-5-nitropyrimidine with two equivalents of the appropriate primary or secondary amine in dry ether as in the following typical experiment.

4-Amino-5-nitro-6-phenethylaminopyrimidine. Phenethylamine (10 g.) in ether (50 ml.) was slowly added to 4-amino-6-chloro-5-nitropyrimidine (7 g.) in ether (200 ml.). After 12 hr. the ether was removed and the residue suspended in water (100 ml.) to remove the phenethylamine hydrochloride. Filtration afforded the essentially pure *product* (9 g., 83%), m. p. 180—181°. Recrystallisation from ethanol gave white plates, m. p. 180—181° (Found: C, 55·8; H, 4·9; N, 26·7. $C_{12}H_{13}O_2N_5$ requires C, 55·5; H, 5·0; N, 27·0%).

The following were prepared similarly: 4-Amino-6-dimethylamino-5-nitropyrimidine (7·3 g., 97%) [from 4-amino-6-chloro-5-nitropyrimidine (7 g.) and 33% w/w methanolic dimethylamine (20 ml.)], pale yellow needles (from ethanol), m. p. 162—163°. Albert *et al.*[6] give m. p. 159—161°. 4-Amino-6-benzylamino-5-nitropyrimidine (3·56 g., 96%) [from 4-amino-6-chloro-5-nitropyrimidine (2·65 g.) and benzylamine (4 g.)], needles, m. p. 202—202·5° (from dioxan) (Found: C, 54·2; H, 4·4. Calc. for $C_{11}H_{11}O_2N_5$: C, 53·8; H, 4·5%). Daly and Christensen [7] give m. p. 191—194°.

4-Amino-6-furfurylamino-5-nitropyrimidine (9·48 g., 98%) [from 4-amino-6-chloro-5-nitropyrimidine (7 g.) and furfurylamine (8 g.)], m. p. 179°, plates from ethanol (Found: C, 46·2; H, 4·2; N, 29·8. $C_9H_9O_3N_5$ requires C, 45·9; H, 3·8; N, 29·7%).

4-Amino-6-cyclohexylamino-5-nitropyrimidine (8·8 g., 96%) [from 4-amino-6-chloro-5-nitropyrimidine (7 g.) and *cyclo*hexylamine (8 g.)], needles (from ethanol), m. p. 203—204° (Found: C, 50·5; H, 6·1; N, 29·4. $C_{10}H_{15}O_2N_5$ requires C, 50·6; H, 6·3; N, 29·5%).

4 : 5-Diamino-6-(substituted amino)pyrimidines.—*4 : 5-Diamino-6-dimethylaminopyrimidine.* 4-Amino-6-dimethylamino-5-nitropyrimidine (5 g.) in ethanol (300 ml.) was shaken with hydrogen in the presence of Raney nickel. Hydrogenation was complete in 30 min. The filtered solution was evaporated *in vacuo* to yield the *product* as pale fawn crystals (3·6 g., 86%), m. p. 156—157°, obtained from benzene as white needles, m. p. 157—158° (Found: C, 47·4; H, 7·0; N, 45·7. $C_6H_{11}N_5$ requires C, 47·0; H, 7·2; N, 45·7%).

4 : 5-Diamino-6-benzylaminopyrimidine. 4-Amino-6-benzylamino-5-nitropyrimidine (1·62 g.) was suspended in boiling water (80 ml.) and treated with sodium dithionite portionwise until the nitro-compound had dissolved. The mixture was made strongly alkaline with aqueous ammonia and cooled in ice. *4 : 5-Diamino-6-benzylaminopyrimidine* (1·22 g., 86%) crystallised

[5] Ziegler-Günder, Simon, and Wacker, *Z. Naturforsch.*, 1956, **11**b, 82; Skinner and Shive, *J. Amer. Chem. Soc.*, 1955, **77**, 6692; Ham, Eakin, Skinner, and Shive, *ibid.*, 1956, **78**, 2648; Skinner, Shive, Ham, Fitzgerald, and Eakin, *ibid.*, p. 5097.

[6] Albert, Brown, and Cheesman, *J.*, 1952, 4228.

[7] Daly and Christensen, *J. Org. Chem.*, 1956, **21**, 177.

and formed needles, m. p. 153—153·5°, from benzene (Found: C, 61·5; H, 5·9; N, 32·9. $C_{11}H_{13}N_5$ requires C, 61·3; H, 6·0; N, 32·5%).

4 : 5-*Diamino*-6-*phenethylaminopyrimidine*.—4-Amino-5-nitro-6-phenethylaminopyrimidine (4 g.) suspended in ethanol (200 ml.) was catalytically reduced as above, to the *base* (3·5 g., 98%), m. p. 200°, needles from methanol (Found: C, 62·7; H, 6·2; N, 30·8. $C_{12}H_{15}N_5$ requires C, 62·8; H, 6·6; N, 30·5%). From 2N-sulphuric acid it yielded the *monosulphate* as needles, m. p. 303° (decomp.) (Found: C, 44·2; H, 5·7; N, 21·4; S, 9·6. $C_{12}H_{15}N_5,H_2SO_4$ requires C, 44·0; H, 5·2; N, 21·4; S, 9·7%).

4 : 5-*Diamino*-6-*furfurylaminopyrimidine*. 4-Amino-6-furfurylamino-5-nitropyrimidine (6 g.) in ethanol (300 ml.) was similarly reduced after which the solution was filtered and evaporated to 15 ml. *in vacuo*. Dilution with four volumes of water and ice-cooling yielded **4 : 5-*diamino*-6-*furfurylaminopyrimidine*** (4·0 g., 76%), forming plates, m. p. 119—119·5°, from benzene (Found: C, 52·7; H, 5·3; N, 34·3. $C_9H_{11}ON_5$ requires C, 52·6; H, 5·4; N, 34·1%). The base (2·5 g.) in ethanol (35 ml.) with concentrated sulphuric acid (1·5 ml.) in water (5 ml.) yielded the *monosulphate* (3·1 g.), plates, m. p. 167—168° (decomp.) (from aqueous ethanol) (Found: C, 35·9; H, 4·4; N, 22·8; S, 10·3. $C_9H_{11}ON_5,H_2SO_4$ requires C, 35·6; H, 4·3; N, 23·1; S, 10·5%).

4 : 5-*Diamino*-6-cyclo*hexylaminopyrimidine*. 4-Amino-6-*cyclo*hexylamino-5-nitropyrimidine (7·5 g.), suspended in ethanol (200 ml.), was catalytically reduced and the filtrate evaporated to dryness *in vacuo* to yield **4 : 5-*diamino*-6-cyclo*hexylaminopyrimidine*** (6·3 g., 98%), plates, m. p. 215° (Found: C, 57·4; H, 7·8; N, 33·9. $C_{10}H_{17}N_5$ requires C, 57·9; H, 8·3; N, 33·8%). Crystallisation of the base (4 g.) from hot 2N-sulphuric acid (150 ml.) yielded the *monosulphate* (4·6 g.), m. p. 198—202° (Found: C, 39·6; H, 6·5; N, 23·4; S, 10·5. $C_{10}H_{17}N_5,H_2SO_4$ requires C, 39·3; H, 6·2; N, 22·9; S, 10·4%).

4-(*Substituted amino*)*pteridines*.—**4-*Dimethylaminopteridine*.** 4 : 5-Diamino-6-dimethylaminopyrimidine (1·6 g.), glyoxal monohydrate (1·6 g.), and water (15 ml.) were heated on a steam-bath for 30 min. Ice-cooling yielded white needles of 4-dimethylaminopteridine (1·5 g., 82%), m. p. 166—167°. Recrystallisation from benzene gave pale yellow prisms, m. p. 168—169° (Found: C, 54·9; H, 4·8; N, 40·2. Calc. for $C_8H_9N_5$: C, 54·8; H, 5·2; N, 39·9%). Albert *et al.*[6] give m. p. 159—161°.

4-*Benzylaminopteridine*. 4 : 5-Diamino-6-benzylaminopyrimidine (1·25 g.), glyoxal monohydrate (2·0 g.), and water (100 ml.) were heated for 15 min. on a steam-bath. The *pteridine* (1·15 g., 72%) was rapidly precipitated and, after ice-cooling, was isolated by filtration. It was obtained from ethanol as pale yellow prisms, m. p. 160—161° (Found: C, 66·0; H 4·3; N, 29·0. $C_{13}H_{11}N_5$ requires C, 65·8; H, 4·6; N, 29·5%).

4-*Phenethylaminopteridine*. 4 : 5-Diamino-6-phenethylaminopyrimidine (2·5 g.), glyoxal monohydrate (3 g.), ethanol (30 ml.) and water (50 ml.) were heated on a steam-bath for 15 min. The mixture was cooled in ice, and the *product* (1·8 g., 65%) removed by filtration. Recrystallisation from ethanol–light petroleum (b. p. 60—80°) yielded pale yellow prisms, m. p. 159—160° (Found: C, 67·0; H, 5·2; N, 28·0. $C_{14}H_{13}N_5$ requires C, 66·9; H, 5·2; N, 27·8%).

4-*Furfurylaminopteridine*. 4 : 5-Diamino-6-furfurylaminopyrimidine (3 g.), glyoxal monohydrate (4 g.), ethanol (20 ml.) and water (40 ml.) were heated on a steam-bath for 30 min. Ice-cooling yielded the *product* (2·25 g., 68%), m. p. 141—142° (from benzene) (Found: C, 58·0; H, 3·9; N, 30·7. $C_{11}H_9ON_5$ requires C, 58·1; H, 3·9; N, 30·8%).

4-cyclo*Hexylaminopteridine*. 4 : 5-Diamino-6-*cyclo*hexylaminopyrimidine (3 g.), glyoxal monohydrate (3 g.), ethanol (30 ml.) and water (30 ml.) were heated on a steam-bath for 30 min. Evaporation of the solution *in vacuo* to half its volume followed by ice-cooling afforded **4-cyclo*hexylaminopteridine*** (3·1 g., 93%), m. p. 105·5—106° (from 10% ethanol), pale yellow needles (Found: C, 62·4; H, 6·2; N, 30·8. $C_{12}H_{15}N_5$ requires C, 62·8; H, 6·6; N, 30·5%).

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827. *Potential Anti-purines. Part II.* The Synthesis of 6- and 9-Substituted Purines and 8-Azapurines.*

By C. L. Leese and G. M. Timmis.

The synthesis is described of a number of purines and their 8-aza-derivatives substituted in the 9- or the 6- and 9-positions, all related to adenine and its riboside.

In the biosynthesis of nucleic acid and certain related co-factors, *e.g.*, purine riboside triphosphates, two routes have been well established in a number of organisms, namely, that starting with glycine amide ribotide and that which utilises a simple purine and converts it in one step into its 9-(ribose phosphate) derivative (ribotide). A third route,[1] involving purine ribosides, *e.g.*, (I), is distinguished from these in being more difficult to discover, and although it therefore appears to be of only minor importance in normal growth it might be important in malignant growth. On this hypothesis we have made analogues of adenine with cyclic substituents at the 9-position (II; R = H) which to some extent simulate sterically the riboside adenosine; these might interfere therefore with the third pathway. In addition, substitution in the amino-group of adenine leads to compounds which have remarkable inhibitory effects on the division of cells in tobacco wound callus tissue in the case of 6-furfurylaminopurine, and on the regeneration of tentacles in hydra in the case of 6-ω-phenylalkylaminopurines.[2] In the hope that an additive or, better, a synergic effect might be obtained we have combined suitable substitution at the 6- and the 9-position of adenine (cf. II). Since replacement of the 8-methine group in purines by nitrogen has yielded compounds with interesting growth-inhibitory properties, *e.g.*, 8-azaguanine, we have also made derivatives of 8-aza-adenine.

The preparation of the intermediate 4 : 5-diamino-6-substituted secondary aminopyrimidines (III; R = phenethyl, *cyclo*hexyl, or furfuryl) is described in the preceding paper. Treatment of these with nitrous acid resulted in ring closure between the 5-amino-group and the secondary amino-group with the formation of 9-substituted 8-aza-adenines (IV; R = NH_2, R′ = phenethyl, *cyclo*hexyl, or furfuryl). In no case was there any evidence for the formation of the isomeric 6-substituted amino-8-azapurines which might have been formed by the alternative mode of ring closure. The products, isolated essentially pure in high yield, were insoluble in alkali, indicating the absence of an acidic triazole-hydrogen atom, a fact which was confirmed by the ultraviolet absorption spectra.

9-Furfuryl-8-aza-adenine has pK_a 2·6 at 22°; the acidic pK_a (which is 5·8 for 8-aza-adenine) is absent, showing that the hydrogen in the triazole ring must be replaced by the furfuryl group. Moreover it was possible to convert one of these 8-aza-adenine derivatives (IV; R = phenethyl) into the 8-azahypoxanthine (IV; R = OH, R′ = phenethyl) by hot nitrous acid. Similar treatment of 9-*cyclo*hexyl- and 9-furfuryl-8-aza-adenine caused extensive decomposition.

The 9-substituted adenine derivatives (II, R = H, R′ = phenethyl, *cyclo*hexyl, or furfuryl) were prepared by formylation and cyclisation of the sulphates of the triaminopyrimidines (III) in formamide at 180°, mixtures with the isomeric 6-(substituted amino)-purines (II; R′ = H) being formed. The 6-(substituted amino)-purines were extracted with N-sodium hydroxide. The identity of these products, formed in minor yield, was finally established by unambiguous synthesis by treatment of 6-methylthiopurine with the appropriate amine.

* Part I, *J.*, 1958, 804.

[1] Aaronson and Rodgriguez, *J. Bacteriol.*, 1957, **74**, 807; Goldthwaite, *J. Clin. Invest.*, 1957, **36**, 1572; Gordon, Intrieri, and Brown, *J. Biol. Chem.*, 1957, **229**, 641; Brockman, Sparks, and Simpson, *Biochim. Biophys. Acta*, 1957, **26**, 671.

[2] Skinner and Shive, *J. Amer. Chem. Soc.*, 1955, **77**, 6692; Ham, Eakin, Skinner, and Shive, *ibid.*, 1956, **78**, 2648; Skinner, Shive, Ham, Fitzgerald, and Eakin, *ibid.*, p. 5097; Skinner, Gardner, and Shive, *ibid.*, 1957, **79**, 2843.

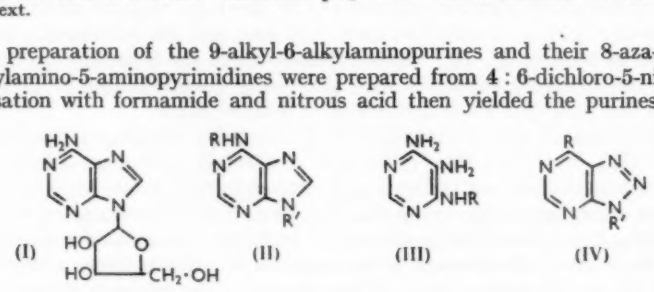
XUM

The structures of the pure 9-substituted adenines were confirmed by the light-absorption data (Table). The spectra are similar to that of adenosine and since the curves remain unaltered between pH 7 and pH 12 the absence of an acidic centre in the glyoxaline ring is confirmed. In contrast the 6-substituted adenines have spectra resembling that of adenine. The pK_a^2 values arise from the ionisation of the glyoxaline-hydrogen atom and the pK_a^1 values represent protonation of a basic centre in the pyrimidine ring.

Compound	pH	$\lambda_{max.}$	$10^{-3}\varepsilon$	$\lambda_{min.}$	$10^{-3}\varepsilon$	pK_a^1	pK_a^2
Adenine	2	263	13·1	229	2·5	2·2	9·8
	12	269	12·3	237	3·35		
6-Phenethylaminopurine	2	273·5	16·2	234	2·82	4·2	10·1
	7	269	17·46	232	2·36		
	12	275	17·7	240	3·57		
6-*cyclo*Hexylaminopurine	2	272	17·1	233	2·5	4·2	10·2
	7	269·5	18·2	230·5	2·14		
	12	275	18·2	241	3·36		
9-*cyclo*Hexyladenine	2	261	14·6	233	3·1	4·19	—
	7—12	262	14·7	229	2·5		
9-*cyclo*Hexyl-6-*cyclo*hexylamino-purine	2	267	17·9	236	2·8	4·4	—
	7—12	271	17·1	234	1·9		
Adenosine	2	257	14·6	230	3·5	3·45	*
	12	260	14·9	227	2·25		
9-Furfuryl-8-aza-adenine	0·9N-HCl	262	12·5	235	5·9	—	—
	5·8—12	279	11·9	236	3·1	†	

* Adenosine exhibits a further dissociation $pK_a^3 = 12·5$ due to ionisation of the sugar moiety.
† See text.

For the preparation of the 9-alkyl-6-alkylaminopurines and their 8-aza-derivatives, 4 : 6-bisalkylamino-5-aminopyrimidines were prepared from 4 : 6-dichloro-5-nitropyrimidine. Cyclisation with formamide and nitrous acid then yielded the purines and 8-aza-



purines respectively in high yield, there being no opportunity for the formation of isomers. The syntheses of 6-*cyclo*hexylaminopurine [3] and 6-amino-9-*cyclo*hexylpurine,[4] from 6-chloropurine and *cyclo*hexylamine and from 6-chloro-9-*cyclo*hexylpurine and ammonia respectively, have recently been described but these methods require the use of pressure vessels and appear to be less convenient than ours.

Experimental

Analyses are by Mr. P. R. W. Baker, Beckenham.

9-Substituted Adenine and 8-Aza-adenine Derivatives.—*9-Phenethyl-8-aza-adenine.* 4 : 5-Diamino-6-phenethylaminopyrimidine (0·5 g.), dissolved in water (10 ml.) containing 2N-hydrochloric acid (2·2 ml.) was treated at 0° dropwise with sodium nitrite (0·19 g.) in water (3 ml.). The *azapurine* (0·45 g., 86%) was precipitated immediately and recrystallised from ethanol yielding white plates, m. p. 218—219° (Found: C, 60·4; H, 4·9; N, 34·8. $C_{12}H_{12}N_4$ requires C, 60·0; H, 5·0; N, 34·9%).

9-Phenethyl-8-azahypoxanthine. 9-Phenethyl-8-aza-adenine (1 g.) in 1·25N-sulphuric acid (60 ml.) at 70° was treated during 10 min. with sodium nitrite (2 g.) in water (10 ml.). The solution was boiled for 5 min., then cooled in ice. A white solid (0·4 g.) separated which from methanol yielded white needles of *9-phenethyl-8-azahypoxanthine*, m. p. 262—263° (Found: C, 60·2; H, 4·7; N, 29·0. $C_{12}H_{11}ON_5$ requires C, 59·7; H, 4·6; N, 29·0%). Neutralisation

[3] Sutherland and Christensen, *J. Amer. Chem. Soc.*, 1957, **79**, 2251.
[4] Montgomery and Temple, *ibid.* 1958, **80**, 409.

of the original filtrate with ammonia yielded unchanged 9-phenethyl-8-aza-adenine (0·5 g.), m. p. 217—218°. Thus there was an 80% conversion of the adenine into the hypoxanthine.

9-*Furfuryl*-8-*aza-adenine*. 4 : 5-Diamino-6-furfurylaminopyrimidine (0·5 g.) in ice-cold water (20 ml.) and 2N-hydrochloric acid (2·5 ml.) was treated with sodium nitrite (0·19 g.) in water (15 ml.) during 10 min. After a further 10 min., 9-*furfuryl*-8-*aza-adenine* (0·5 g., 95%) was removed by filtration and obtained as white plates, m. p. 227—228°, from ethanol (Found: C, 50·0; H, 3·6; N, 38·8. $C_9H_8ON_6$ requires C, 50·0; H, 3·7; N, 38·8%).

9-cyclo*Hexyl*-8-*aza-adenine*. 4 : 5-Diamino-6-*cyclo*hexylaminopyrimidine (1·5 g.) in water (100 ml.) and 2N-hydrochloric acid (7·3 ml.) with sodium nitrite (0·55 g.) in water (10·0 ml.) as before gave the *aza-adenine* (1·5 g., 95%), plates, m. p. 264—265° (from ethanol) (Found: C, 55·3; H, 6·2; N, 38·4. $C_{10}H_{14}N_6$ requires C, 55·0; H, 6·5; N, 38·5%). Attempted conversion into the hypoxanthine resulted in 80% recovery of the starting material. Prolonged treatment with hot nitrous acid caused decomposition.

9-*Phenethyladenine*. 4 : 5-Diamino-6-phenethylaminopyrimidine sulphate (1·7 g.) and formamide (5 ml.) were heated at 180—190° for 20 min., cooled, and diluted with water (50 ml.). The solid (1·4 g.), m. p. 150—163°, which was isolated was suspended in 2N-sodium hydroxide (15 ml.), warmed for 1 min. on a steam-bath, cooled, and filtered. The residue (1·05 g., 84%), on recrystallisation from aqueous ethanol, yielded 9-*phenethyladenine*, m. p. 179—180° (Found: C, 65·2; H, 5·5; N, 29·3. $C_{13}H_{13}N_5$ requires C, 65·2; H, 5·5; N, 29·2%). Neutralisation of the alkaline extract with acetic acid yielded 6-phenethylaminopurine (0·2 g., 11%), m. p. 245—246°, identical with a sample prepared by heating 6-methylthiopurine with phenethylamine (Skinner *et al.*, 1956, ref. 2).

9-*Furfuryladenine*. 4 : 5-Diamino-6-furfurylaminopyrimidine sulphate (5 g.) in formamide (12 ml.) gave similarly 9-*furfuryladenine* (1·3 g., 37%), m. p. 190—191°, needles from ethanol (Found: C, 55·9; H, 4·3; N, 32·3. $C_{10}H_9ON_5$ requires C, 55·8; H, 4·2; N, 32·5%). The alkaline extract on neutralisation with acetic acid deposited 6-furfurylaminopurine (kinetin) (0·35 g., 10%), m. p. 269—270°, identical with a specimen prepared by heating 6-methylthiopurine with furfurylamine.

9-cyclo*Hexyladenine*. 4 : 5-Diamino-6-*cyclo*hexylaminopyrimidine sulphate (2·35 g.) in formamide (6 ml.) yielded 9-*cyclo*hexyladenine,[4] m. p. 197—198°, plates from benzene (Found: C, 61·3; H, 6·8; N, 32·5. Calc. for $C_{11}H_{15}N_5$: C, 60·8; H, 6·9; N, 32·2%). This afforded a *picrate* (from saturated ethanolic picric acid), m. p. 295° (decomp.) (Found: N, 25·0. $C_{17}H_{18}O_7N_8$ requires N, 25·1%). Acidification of the alkaline extract with acetic acid yielded a trace of crystals, m. p. 205—206°, identical with 6-*cyclo*hexylaminopurine (see below).

6-cyclo*Hexylaminopurine*. 6-Methylthiopurine (0·8 g.), *cyclo*hexylamine (1 g.), and water (2 ml.) were heated at 150° for 24 hr. in a sealed tube, then on a steam-bath to expel methanethiol, and treated with water (10 ml.) and adjusted to pH 5 with acetic acid. Ice-cooling yielded a white solid (0·6 g.) which gave 6-*cyclo*hexylaminopurine [3] (0·4 g., 38%), m. p. 206—207°, as needles from methanol (Found: C, 61·2; H, 7·0; N, 32·2. Calc. for $C_{11}H_{15}N_5$: C, 60·8; H, 6·9; N, 32·2%). The *picrate*, from ethanolic picric acid, was obtained as yellow needles (from water), m. p. 242—243° (Found: N, 23·8. $C_{17}H_{16}O_7N_8,H_2O$ requires N, 24·2%).

5-*Nitro*-4 : 6-*di*(*phenethylamino*)*pyrimidine*. 4 : 6-Dichloro-5-nitropyrimidine [5] (5 g.) in ether (200 ml.) was slowly treated with phenethylamine (16 g.) in ether (20 ml.). After 18 hr. the ether was removed *in vacuo* and the solid residue extracted with water (100 ml.). The *product* (8·15 g., 87%) was isolated and obtained from light petroleum (b. p. 60—80°) as pale yellow needles, m. p. 133—134° (Found: C, 66·1; H, 5·9; N, 18·9. $C_{20}H_{21}O_2N_5$ requires C, 66·1; H, 5·8; N, 19·2%).

4 : 6-*Di*(*furfurylamino*)-5-*nitropyrimidine*. This *compound* (7·74 g., 95%) was obtained by the general method from 4 : 6-dichloro-5-nitropyrimidine (5 g.) and furfurylamine (13 g.). Recrystallisation from benzene–light petroleum (b. p. 80—100°) gave white needles, m. p. 132—133° (Found: C, 53·4; H, 4·3; N, 21·9. $C_{14}H_{13}O_4N_5$ requires C, 53·3; H, 4·1; N, 22·2%).

4 : 6-*Di*(cyclo*hexylamino*)-5-*nitropyrimidine*. This *compound* (6·47 g., 78%) was similarly obtained from 4 : 6-dichloro-5-nitropyrimidine (5 g.) and *cyclo*hexylamine (13 g.). It formed pale yellow needles, m. p. 135—136°, from light petroleum (b. p. 80—100°) (Found: C, 60·2; H, 7·9; N, 21·8. $C_{16}H_{25}O_2N_5$ requires C, 60·1; H, 7·9; N, 21·9%).

5-*Amino*-4 : 6-*di*(*phenethylamino*)*pyrimidine*. 5-Nitrodi(phenethylamino)pyrimidine (8·17 g.), suspended in ethanol (300 ml.), was reduced with hydrogen and Raney nickel and the filtrate

[5] Boon, Jones, and Ramage, *J.*, 1951, 96.

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evaporated to dryness *in vacuo* to yield the *product* (7·5 g., 95%), m. p. 126—127°. It was obtained from benzene–light petroleum (b. p. 60—80°) as white plates, m. p. 131—131·5° (Found: C, 71·9; H, 6·8; N, 21·2. $C_{20}H_{22}N_8$ requires C, 72·0; H, 6·9; N, 21·0%).

5-Amino-4 : 6-di(furfurylamino)pyrimidine. 4 : 6-Difurfurylamino-5-nitropyrimidine (6·13 g.) in ethanol (200 ml.) similarly gave this *product* (4·90 g., 88%), plates, m. p. 117° [from light petroleum (b. p. 60—80°)] (Found: C, 59·1; H, 5·3; N, 24·8. $C_{14}H_{15}O_2N_5$ requires C, 58·9; H, 5·3; N, 24·5%).

5-Amino-4 : 6-di(cyclohexylamino)pyrimidine. This *compound* (4·15 g., 81%) was similarly obtained by the catalytic hydrogenation of 4 : 6-di(*cyclo*hexylamino)-5-nitropyrimidine (5·64 g.) in ethanol (200 ml.). It was purified by dissolution in dilute acetic acid and precipitation with dilute ammonia, yielding white prisms, m. p. 299—300° (Found: C, 66·3; H, 9·1; N, 24·4. $C_{16}H_{27}N_5$ requires C, 66·4; H, 9·4; N, 24·2%).

9-Substituted 6-(Substituted amino)-purines and -8-aza-purines.—*9-Phenethyl-6-phenethylamino-8-azapurine.* 5-Amino-4 : 6-di(phenethylamino)pyrimidine (1 g.) in glacial acetic acid (20 ml.) and water (10 ml.) was cooled in ice and treated dropwise with sodium nitrite (0·25 g.) in water (1 ml.). The precipitated *azapurine* (0·77 g., 74%) yielded white needles, m. p. 201°, from ethanol (Found: C, 69·6; H, 5·5; N, 24·6. $C_{20}H_{20}N_6$ requires C, 69·7; H, 5·8; N, 24·4%).

9-Furfuryl-6-furfurylamino-8-azapurine. This *compound* (0·93 g., 89%) was obtained when 5-amino-4 : 6-di(furfurylamino)pyrimidine (1 g.) in glacial acetic acid (5 ml.) and water (25 ml.) was treated with sodium nitrite (0·25 g.) in water (2 ml.) as in the previous experiment. The pure compound, m. p. 125—126°, obtained from ethanol exhibited dimorphism (Found: C, 56·4; H, 4·0; N, 28·7. $C_{14}H_{12}O_2N_6$ requires C, 56·7; H, 4·0; N, 28·3%).

9-cyclohexyl-6-cyclohexylamino-8-azapurine. This *azapurine* (0·95 g., 91%) was similarly obtained from 5-amino-4 : 6-di(*cyclo*hexylamino)pyrimidine (1 g.) in glacial acetic acid (15 ml.) and water (15 ml.) by sodium nitrite (0·25 g.) in water (2 ml.). Recrystallisation from aqueous ethanol yielded prisms, m. p. 166—167° (Found: C, 63·8; H, 7·9; N, 28·1. $C_{16}H_{24}N_6$ requires C, 63·9; H, 8·0; N, 27·9%).

9-Phenylethyl-6-phenylethylaminopurine hydrochloride. 5-Amino-4 : 6-di(phenethylamino)-pyrimidine (0·5 g.) in formamide (2 ml.) containing 1 drop of concentrated sulphuric acid was heated at 180—190° for 10 min. The cooled mixture was diluted with ethanol (5 ml.) and poured into 18% w/v hydrochloric acid (30 ml.). After ice-cooling the crystalline *purine hydrochloride* was filtered off and recrystallised from 2N-hydrochloric acid as plates (0·35 g., 60%), m. p. 230—231° (Found: C, 66·7; H, 5·8; N, 18·7; Cl, 8·9. $C_{21}H_{21}N_5$,HCl requires C, 66·3; H, 5·8; N, 18·4; Cl, 9·3%).

9-Furfuryl-6-furfurylaminopurine. 5-Amino-4 : 6-di(furfurylamino)pyrimidine (1 g.) was heated at 180—190° for 15 min. in formamide (3 ml.) containing formic acid (0·5 ml.). Dilution with water (30 ml.) and ice-cooling yielded the *purine* (0·97 g., 91%), needles, m. p. 128·5—129° from benzene–light petroleum (b. p. 60—80°) (Found: C, 61·0; H, 4·3; N, 23·9. $C_{15}H_{13}O_2N_5$ requires C, 61·0; H, 4·4; N, 23·7%).

9-cyclohexyl-6-cyclohexylaminopurine hydrochloride. 5-Amino-4 : 6-di(*cyclo*hexylamino)-pyrimidine (0·5 g.) was heated with formamide (3 ml.) and formic acid (0·2 ml.) at 180—190° for 25 min. The cooled mixture was dissolved in ethanol (3 ml.) and poured into water (40 ml.) containing aqueous ammonia (5 ml.; *d* 0·88). Ice-cooling caused slow solidification of the oily product which then was dissolved in ethanol (10 ml.) and saturated with dry hydrogen chloride, to yield a white crystalline hydrochloride (0·45 g.), m. p. 226—229°. This was purified twice by dissolution in ethanol and saturation of the solution with dry hydrogen chloride, to yield needles of the pure *salt* (0·40 g., 68%), m. p. 233—235° (Found: C, 59·9; H, 7·8; N, 20·6; Cl, 11·0. $C_{17}H_{25}N_5$,HCl requires C, 60·7; H, 7·8; N, 20·8; Cl, 10·5%).

We are very much indebted to Dr. P. D. Lawley for light-absorption data and to Mr. D. Manners for technical assistance. This work has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

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828. *Solvation of Calcium Nitrate and of Lithium Perchlorate in Acetone Solution measured by an Ultrasonic Method.*

By P. G. T. Fogg.

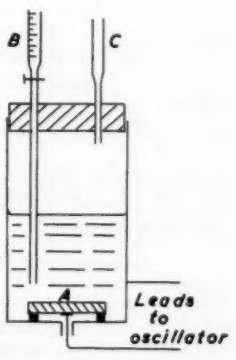
Evidence for the formation of complexes when calcium nitrate or lithium perchlorate is dissolved in acetone has been obtained by measuring the ultrasonic velocity in the solutions. Spectroscopy has yielded additional evidence for the formation of acetone–calcium nitrate complexes in sclution. A simple instrument for measuring the velocity of sound in liquids is described.

The degree of solvation of a salt can be related to the compressibility of the solution and hence to the velocity of sound in the solution, by Passynsky's method.[1] The degrees of hydration of numerous salts have been so measured;[2] the values obtained are comparable with those obtained by other methods.[3] There is spectroscopic evidence for solvation of salts in non-aqueous solutions[4] but there have been few quantitative measurements of degrees of solvation.

The degree of solvation of lithium perchlorate and of calcium nitrate at various concentrations in acetone has now been measured.

Experimental

Materials.—Hydrated calcium nitrate (B.D.H.) was dehydrated at 170°. Lithium perchlorate was prepared from lithium carbonate (B.D.H.) by neutralising it with a slight excess of "AnalaR" 72% perchloric acid. The mixture was digested on a hot-plate until evolution of carbon dioxide ceased and a clear solution resulted. Excess of acid and water were removed by heating *in vacuo* at 150°. "AnalaR" acetone was dehydrated by anhydrous calcium sulphate.



Apparatus.—The velocity of sound in different liquids was compared by use of an acoustic interferometer in which the surface of the liquid serves as reflector (see Figure). A similar method has been used previously.[5]

A quartz crystal *A* of fundamental frequency *ca.* 1000 kc./sec. is made to oscillate by a circuit of the Pierce type. Changes in the power needed cause changes in the anode current of the valve in the oscillating circuit which are measured by a mirror galvanometer in a potentiometer circuit. The crystal is fixed in a holder of the Gutmann type[6] (not shown in detail) which is screwed into a brass cylinder with uniform bore. The joint is sealed by a gasket. The cylinder is securely clamped so that the crystal is level. Liquid under test can be run into the cylinder from a burette *B* with an elongated tip. The top of the cylinder is fitted with a rubber bung and drying tube *C*. The burette is also fitted with a drying tube.

Sound waves are reflected from the surface of the liquid and at certain levels of liquid the anode current reaches a sharp maximum. This occurs when the distance between liquid surface and crystal surface is equal to $\frac{1}{2}n\lambda + \frac{1}{4}\lambda$ where n is an integer and λ the wavelength of the sound. The distance between two such positions is equal to $\lambda/2$.

Twenty consecutive burette readings r for maximum current are recorded. The average

[1] Passynsky, *Acta Physicochim. U.R.S.S.*, 1938, **8**, 835.
[2] Giacomini and Pesce, *Ricerca sci.*, 1940, **11**, 605.
[3] Bockris, "Modern Aspects of Electrochemistry," Butterworths Scientific Publications, London, 1954, p. 62; Bell, *Endeavour*, 1958, **17**, 31.
[4] Pullin and Pollock, *Trans. Faraday Soc.*, 1958, **54**, 11.
[5] Hunter and Fox, *J. Acoustical Soc. Amer.*, 1950, **22**, 238.
[6] Gutmann, *J. Sci. Instr.*, 1947, **24**, 276.

difference between two consecutive readings, which is proportional to $\lambda/2$, is calculated from the relation:

$$\text{Average} = \left(\sum_{n=11}^{n=20} r - \sum_{n=1}^{n=10} r\right)/100$$

Measurements are reproducible to about 1 part in 2000, showing that the frequency remains constant. Velocities of sound in different liquids are therefore proportional to the difference between two consecutive readings.

An ordinary density bottle was used to measure densities of liquids.

The room temperature was maintained at 17° ± 0·1°.

A Perkin-Elmer model 21 spectrometer was used to investigate the spectra of calcium nitrate solutions.

Results and Discussion

Results are tabulated. Values for the velocity of sound and the compressibility are relative to those for pure acetone at the same temperature.

The adiabatic compressibility β is related to the density d and the velocity of sound v by the equation $\beta = 1/v^2d$. On account of electrostriction, molecules in the solvation sheath will be highly compressed so that these molecules will be less compressible than those in the bulk of the solution when an external pressure is applied. Hence the bulk compressibility of the solution is less than that of the pure solvent. Passynsky [1] assumed that molecules very near to the ion in the primary solvation sheath have zero compressibility. If the bulk compressibility of the solvent is represented by β_0, the compressible volume of the solution by V, and the incompressible volume of the solvation sphere by u, then

$$\beta_0 = \frac{1}{V-u}\left(\frac{\partial(V-u)}{\partial P}\right)_T = \frac{1}{V-u}\left(\frac{\partial V}{\partial P}\right)_T$$

and

$$\beta = \frac{1}{V}\left(\frac{\partial V}{\partial P}\right)_T$$

Hence $\beta/\beta_0 = (V-u)/V = (V-\alpha V)/V$ where $\alpha = u/V$

or $\alpha = 1 - \beta/\beta_0$

If there are n_2 moles of solute and n_1 moles of solvent there are $\alpha n_1/n_2$ moles of incompressible solvent per mole of solute. This may be identified with the primary solvation number of the salt.

Concn. (M)	Velocity of sound	d (g./c.c.)	β	Solvation no.	Concn. (M)	Velocity of sound	d (g./c.c.)	β	Solvation no.
	Calcium nitrate					*Lithium perchlorate*			
0·0136	0·999	0·8204	0·972	2·03	0·0142	1·014	0·8140	0·951	3·40
0·0317	1·001	0·8522	0·932	2·00	0·0336	1·028	0·8364	0·900	2·87
0·0549	1·002	0·8950	0·885	1·97	0·0619	1·057	0·8742	0·814	2·83
0·0891	1·030	0·9576	0·782	2·06	0·1169	1·111	0·9518	0·738	2·44
0·1601	1·113	1·0784	0·594	2·12	0·1847	1·176	1·0314	0·558	1·95
					0·2181	1·207	1·0836	0·504	1·78
					0·3348	1·253	1·2196	0·416	1·16

The solvation number of calcium nitrate is 2, to the nearest whole number, and does not vary significantly with concentration. This is in accord with the formation of a stable complex with two molecules of acetone associated with one calcium ion. Crystals of an acetone complex will gradually settle from a concentrated solution of calcium nitrate in acetone. Some of these crystals were filtered off in a dry atmosphere, dried between filter papers, and analysed by finding the proportion of acetone lost *in vacuo*. The molar ratio acetone : salt was 1·9. A little bound acetone may have been lost during filtration and drying.

The solvation number of lithium perchlorate varies from 1·2 to 3·4 in the concentration range studied. This is in accord with the existence of an equilibrium mixture of unsolvated ions, acetone molecules, and ions of different degrees of solvation. The results show that at infinite dilution the solvation number would be about 4.

A preliminary investigation of the infrared absorption spectra of calcium nitrate solutions showed that the 1225 cm.$^{-1}$ acetone band is split into two components at about 1224 cm.$^{-1}$ and 1237 cm.$^{-1}$ and that the 1715 cm.$^{-1}$ band becomes complex in saturated solution and in 0·1334M-solution. The relative intensity of the 1237 cm.$^{-1}$ band is greater in the saturated than in the weaker solution. Similar changes of these acetone bands have been reported by Pullin and Pollock [4] in the spectra of silver perchlorate and lithium perchlorate solutions. They have been explained as being due to the formation of acetone complexes. The changes in the spectra of calcium solutions are probably also due to complex formation.

Pullin and Pollock have shown that, in 0·3M-lithium perchlorate solution, the acetone is almost completely associated, presumably as $Li^+(acetone)_2$ (solvation no. 2). Interpolation of the results quoted above gives a solvation number of 1·35 at this concentration. This difference may show that the neglect of the compressibility of complexes in concentrated solutions is not completely justified.

The fact that lithium ions appear to be more solvated than calcium ions at infinite dilution may be related to a difference in mode of formation of complexes in the two cases. Another possibility is that perchlorate ions are solvated in these solutions although anions are not usually solvated.

The author is indebted to Dr. A. D. E. Pullin for assistance in the spectroscopy.

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829. *Unsaturated Systems. Part II.* The Reactivity of α-Chlorocrotonic and α-Chloro-β-methylcrotonic Acid.*

By M. U. S. SULTANBAWA and P. VEERAVAGU.

The difference in reactivity between α-chloro- and α-bromo-crotonic acid towards methanolic sodium methoxide is held to be mainly due to the lower solubility of sodium α-chlorocrotonate in the reaction medium. The behaviour of α-chloro-β-methylcrotonic acid towards methanolic sodium methoxide and aqueous sodium hydroxide is similar to that of α-bromo-β-methylcrotonic acid.

α-BROMOCROTONIC ACID with methanolic sodium methoxide gives α-methoxycrotonic acid.[1] However, it was reported by Owen and Sultanbawa [2] that the chlorine atom of α-chlorocrotonic acid is replaced if alkali of sufficient concentration is used, in contrast to earlier observations.[3] α-Chlorocrotonic acid in an excess of *ca.* 2·5N-methanolic sodium methoxide formed a heterogeneous mixture which after refluxing for 24 hours gave α-methoxycrotonic acid in 58% yield, together with a small amount of oil. The oil could have been formed by the addition of methanol to α-methoxycrotonic acid, and when this acid was heated with 2·5N-sodium methoxide for 22 hours and the product purified by means of alkaline permanganate a liquid was obtained which on analytical evidence (carbon and hydrogen) may have contained some αβ-dimethoxybutyric acid (cf. refs. 1 and 4).

* The paper by Alles and Sultanbawa, *J.*, 1956, 3472, is considered as Part I of the series.

[1] Owen, *J.*, 1945, 385.
[2] Owen and Sultanbawa, *J.*, 1949, 3089.
[3] Sarnow, *Annalen*, 1872, **164**, 96; Kahlbaum, *Ber.*, 1879, **12**, 2338; Friedrich, *Annalen*, 1883, **219**, 322.
[4] Owen and Somade, *J.*, 1947, 1030.

In its reactions with the higher alkoxides, α-chloro- was similar to α-bromo-crotonic acid, but only the addition products β-ethoxy-, β-*iso*propoxy-, and β-*tert.*-butoxy-crotonic acid [1] could be characterised.

The difference in reactivity of the chloro- and the bromo-crotonic acid was not directly determined as the chloro-acid gave a heterogeneous reaction medium. However, it was found that sodium α-bromocrotonate was nearly 1·4 times more soluble in methanol and nearly 4 times more soluble in methanolic 3·5N-sodium methoxide (the approximate concentration at the start of the reaction) than sodium α-chlorocrotonate. The solubility difference may, therefore, in our opinion, be an important factor (cf. α-chloro-β-methylcrotonic acid below) in the different reactivities.

To extend the study, α-chloro-β-methylcrotonic-acid was prepared by adding chlorine to β-methylcrotonic acid with sulphuryl chloride [5] as all attempts to add chlorine directly failed (crotonic acid failed to react) and converting the αβ-dichloro-β-methylbutyric into α-chloro-β-methylcrotonic acid by treatment with ethanolic sodium ethoxide (cf. ref. 2). This acid gave a homogeneous solution with *ca.* 4N-methanolic sodium methoxide. Its reactivity and that of the corresponding bromo-acid towards sodium methoxide are shown in Table 1. The reaction rates—the net effect of prototropy and replacement at an allylic centre—are almost equal. That the mechanisms of the two reactions are similar was shown by the isolation in 80% yield of an unsaturated acid mixture, the light absorption of which showed that it contained only 19% of α-methoxy-β-methylcrotonic acid but which was converted in 77% yield into α-methoxy-β-methylcrotonic acid by hot aqueous *ca.* 5N-sodium hydroxide in 24 hours.

The reaction of the α-chloro-β-methylcrotonic acid with aqueous sodium hydroxide was shown quantitatively to be very similar to that of the bromo-acid [2] (see Table 2). In keeping with this the chloro-acid, on treatment with aqueous 2N-sodium hydroxide gave both β-methyl-α-oxobutyric and γ-hydroxy-β-methylcrotonic acid, the formation of the latter, as in the bromo-series, indicating the occurrence of anionotropy as well as of prototropy.

Experimental

αβ-Dichlorobutyric acid [6] was converted into α-chlorocrotonic acid,[7] m. p. 99·5°, by means of pyridine.

Reaction of α-Chlorocrotonic Acid with Sodium Methoxide.—The heterogeneous mixture of the acid (6·0 g.), methanol (50 c.c.), and methanolic 5·2N-sodium methoxide (75 c.c.) was refluxed for 24 hr. (preliminary experiments showed 98% reaction). After removal of the solvent, the residue was dissolved in water, cooled, acidified with 6N-hydrochloric acid, and extracted with ether. The extracts were dried ($CaCl_2$) and evaporated. The semisolid residue (3·3 g., 58%) was filtered off and a few drops of a liquid, n_D^{29} 1·4275, were collected. The solid was α-methoxycrotonic acid, m. p. and mixed m. p. 58° [*S-benzylthiuronium salt*, m. p. 168—169° (from ethanol) (Found: C, 55·2; H, 6·5; N, 9·8. $C_{13}H_{18}O_3N_2S$ requires C, 55·3; H, 6·8; N, 9·7%)].

Reaction of α-Methoxycrotonic Acid with Sodium Methoxide.—α-Methoxycrotonic acid (5 g.) was heated on a water-bath for 22 hr. with methanolic 2·5N-sodium methoxide (105 c.c.) and worked up as above, giving a pale yellow mobile liquid (4·3 g.), $\lambda_{max.}$ 218 mμ (ε 4700) in ethanol, *i.e.*, containing *ca.* 50% of αβ-unsaturated acid. By fractionation were separated (*a*) α-methoxycrotonic acid (1·9 g.), (*b*) a liquid (1·8 g.), b. p. 59—62°/0·35 mm., n_D^{29} 1·4250—1·4380, $\lambda_{max.}$ 219 mμ (ε 3000—3400) in ethanol.

The liquid (1·8 g.) in dilute aqueous sodium carbonate was treated with 3% aqueous potassium permanganate (10 c.c.) at 5° with stirring during 15 min.; the precipitate was filtered off and washed with water, and the filtrate was cooled, acidified, and extracted with ether. On removal of the ether from the dried extracts ($CaCl_2$), a colourless liquid (0·8 g.) was obtained, having $\lambda_{max.}$ 218 mμ (ε 350) (*ca.* 4% of αβ-unsaturated acid). It was distilled into

[5] Kharasch and Brown, *J. Amer. Chem. Soc.*, 1939, **61**, 3432.
[6] Michael and Bunge, *Ber.*, 1908, **41**, 2910.
[7] Pfeiffer, *Ber.*, 1910, **43**, 3041.

fractions: (1) b. p. 90—94°/9 mm., n_D^{29} 1·4180 (0·1 g.); (2) b. p. 94—98°/9 mm., n_D^{29} 1·4310 (0·3 g.) [Found for fraction (1): C, 49·9; H, 8·1. For fraction (2): C, 49·7; H, 7·65. Calc. for $C_5H_8O_3$ (α-methoxycrotonic acid): C, 51·7; H, 6·9. Calc. for $C_6H_{12}O_4$ (αβ-dimethoxybutyric acid): C, 48·6; H, 8·2%].

Reaction of α-Chlorocrotonic Acid with Sodium Ethoxide.—The heterogeneous mixture of the acid (6·0 g.) and ethanolic 2·6N-sodium ethoxide (250 c.c.) was heated on the steam-bath for 23 hr. (preliminary experiments showed 96% reaction). The product was isolated as a dark brown viscous oil (2·2 g.) which deposited some β-ethoxycrotonic acid (0·12 g.), m. p. 140° (from aqueous methanol), at 0°. Attempts to isolate other products failed.

Reaction of α-Chlorocrotonic Acid with Potassium iso*Propoxide.*—The acid (3·6 g.) was heated with a solution of potassium (10 g.) in propan-2-ol (100 c.c.) on a steam-bath for 24 hr. and the product worked up as above. A methanolic extract of the dark brown semisolid product (0·2 g.) gave a few crystals of β-*iso*propoxycrotonic acid, m. p. 105—106°.

Solubility of Sodium α-Chlorocrotonate and α-Bromocrotonate.—(A) *Methanol.* (1) Sodium α-chlorocrotonate was refluxed with methanol for 5 min. and the amount of salt dissolved in 15 c.c. of the solution determined. The solubility was found to be 92·3 g./l. (0·648 equiv./l.). (2) The solubility of sodium α-bromocrotonate was similarly found to be 166·5 g./l. (0·890 equiv./l.).

(B) *Methanolic 3·5N-sodium methoxide.* (1) Sodium α-chlorocrotonate was refluxed with 3·5N-sodium methoxide for 5 min., the undissolved salt was allowed to precipitate, 10 c.c. of the hot supernatant liquid were removed and heated under reflux for 24 hr. and the halide ion produced was estimated volumetrically. The solubility was thus found to be 9·16 g./l. (0·064 equiv./l.).

(2) A similar experiment gave the solubility of sodium α-bromocrotonate as 49·65 g./l. (0·266 equiv./l.).

Addition of Chlorine to β-Methylcrotonic Acid with Sulphuryl Chloride.[5]—Freshly crystallised β-methylcrotonic acid (100 g.) and benzoyl peroxide (0·2 g.) in carbon tetrachloride (200 c.c.) were refluxed and sulphuryl chloride (90 c.c., *ca.* 8% excess) in carbon tetrachloride (100 c.c.) was added during an hour. On removal of the solvent after a further 6 hours' refluxing, a colourless viscous oil was obtained having b. p. 78—80°/0·033 mm., n_D^{29} 1·4660—1·4698 (148 g., 78%). Some of the fractions on storage deposited αβ-*dichloro*-β-*methylbutyric acid*, which crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. 48—49° (Found: C, 35·4; H, 4·7; Cl, 41·4. $C_5H_8O_2Cl_2$ requires C, 35·1; H, 4·7; Cl, 41·5%) [S-*benzylthiuronium salt*, needles (from aqueous alcohol), m. p. 120° (decomp.) (Found: N, 8·3. $C_{13}H_{18}O_2Cl_2N_2S$ requires N, 8·65%)].

Under the above conditions or with 50% excess of sulphuryl chloride or refluxing for 24 hr. addition of chlorine to crotonic acid could not be effected.

Preparation of α-Chloro-β-methylcrotonic Acid.—To a cooled solution of αβ-dichloro-β-methylbutyric acid (35 g.) in ethanol (100 c.c.) was added, with stirring, 4N-sodium ethoxide (100 c.c.) in 15 min., the temperature being kept below 5°. The mixture was kept at 0° for 10 hr., then heated on a water-bath for 30 min., and the solvent was removed. The residue was dissolved in water and extracted with ether. The aqueous solution was then acidified and extracted with ether, and the extracts dried (Na_2SO_4) and evaporated. The residue (18·5 g., 68%) of α-chloro-β-methylcrotonic acid crystallised in needles (from water), 85—86° (lit.,[8] m. p. 85—86°).

Comparison of the Reactivities of α-Chloro-β-methylcrotonic and α-Bromo-β-methylcrotonic Acid.—(*a*) α-Chloro-β-methylcrotonic acid (1·350 g.) was dissolved in methanol and the solution made up to 50 c.c. Portions (4 c.c.) of this solution were run into Pyrex test tubes containing methanolic 3·7N-sodium methoxide (2 c.c.). The tubes were sealed and kept in a boiling-water bath. At intervals, the tubes were removed and the cooled contents poured into water and acidified with 4N-nitric acid, and any unchanged chloro-acid was extracted with ether. The chloride ion in the aqueous solution was determined volumetrically (Volhard's method). The results are given in Table 1.

(*b*) A similar determination with α-bromo-β-methylcrotonic acid (1·80 g.) in methanol (50 c.c.) is also shown in Table 1.

Reaction of α-Chloro-β-methylcrotonic Acid with Sodium Methoxide.—The acid (3·5 g.) in methanol (50 c.c.) was refluxed with methanolic 4·3N-sodium methoxide (120 c.c.) for 10 hr.

[8] Prentice, *Annalen*, 1896, **292**, 275.

The product (10·2 g., 80%), worked up as in the case of the bromo-acid,[2] had b. p. 51—54°/3·6 × 10^{-3} mm., n_D^{29} 1·4465—1·4520, $\lambda_{max.}$ 228 mμ (ε 1460—2320) in EtOH, *i.e.*, it contained about 19% of α-methoxy-β-methylcrotonic acid, the rest being the βγ-unsaturated isomer.

The mixed acids (1·0 g.) were heated with aqueous 4·9N-sodium hydroxide (10 c.c.) for 24 hr. on the steam-bath and worked up as above. α-Methoxy-β-methylcrotonic acid (0·77 g.), m. p. and mixed m. p. 70·5°, was obtained.

TABLE 1.

	α-Chloro-β-methylcrotonic acid.						*α-Bromo-β-methylcrotonic acid.*						
Time (hr.) ...	0·5	1·0	3·0	5·5	9·0	11·0	0·5	1·5	2·5	4·0	6·0	8·5	10·0
Reaction (%)	18·0	34·1	72·5	88·2	97·0	98·6	21·5	51·0	65·3	83·0	94·5	98·5	99·2

Action of Aqueous Sodium Hydroxide on α-Chloro-β-methylcrotonic Acid.—(1) The chloro-acid (1·35 g.) was made up to 50 c.c. with aqueous 1·017N-sodium hydroxide and heated under reflux on a steam-bath. At intervals, 5 c.c. portions were removed and titrated against 0·1000N-hydrochloric acid. The results are given in Table 2.

TABLE 2.

Time (hr.)	1	2	4	6	8	10	12	24
1·017N-NaOH								
Cl^- liberated (%)	—	33	48	61	72	79	81	85
Keto-acid formed (%)	—	1	2·5	4	5·5	7·5	10	20
2·03N-NaOH								
Cl^- liberated (%)	59	80	92	98	102	102	—	—
Keto-acid formed (%)	—	5	10·5	17·5	21	25	27·5	34

The solution from each titration was treated with excess of 1% 2 : 4-dinitrophenylhydrazine in 4N-sulphuric acid (40 c.c.). The precipitated 2 : 4-dinitrophenylhydrazone of γ-methyl-α-oxobutyric acid was filtered off, dried, and weighed. The results are given in Table 2.

(2) A similar experiment to (1) with the chloro-acid (1·35 g.) in aqueous 2·034N-sodium hydroxide (made up to 50 c.c.) is also in Table 2.

Reaction of α-Chloro-β-methylcrotonic Acid with Aqueous Sodium Hydroxide.—The acid (5·0 g.) in aqueous 2N-sodium hydroxide (125 c.c.) was heated on a steam-bath for 9 hr. and the product (3·35 g., 78%) was worked up as for the bromo-acid.[2] The product on distillation gave β-methyl-α-oxobutyric acid, b. p. 72—75°/18 mm., n_D^{29} 1·4145 (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 194°). From the residue, by distillation in a retort, two fractions were collected at bath-temperature 110—130°/3·6 × 10^{-3} mm.: (1) 0·18 g., n_D^{29} 1·4535; (2) 0·55 g., n_D^{29} 1·4715. In the trap γ-methyl-α-oxobutyric acid (0·75 g.) was also collected. Fraction (2) at 0° deposited a small amount of γ-hydroxy-β-methylcrotonic acid, m. p. and mixed m. p. 112—113° (hot stage).

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830. *Electrometric Titration of the Sodium Salts of Deoxyribonucleic Acids. Part VI.* The Forward-titration Curve.*

By R. A. Cox and A. R. Peacocke.

Dissociation curves have been obtained at 25° in 0·05M-sodium chloride for a neutral solution of herring-sperm sodium deoxyribonucleate titrated with acid to a series of pH values higher than that corresponding to complete denaturation and then back-titrated to neutrality. Thence is derived the relation between the proportion (β) of the original double-helical structure which became disordered and the degree of ionisation (γ) of the initially hydrogen-bonded amino-groups. Below a critical value of γ this relation follows closely that predicted on the assumption that co-operative ionisation of two adjacent hydrogen-bonded groups is the necessary condition for the disordering of any part of the original structure. At the critical value of γ (*viz.*, $\gamma = 0{\cdot}75$, when $\beta = 0{\cdot}75$) there is apparently a sudden breakdown of the remaining hydrogen-bonded structure into a completely disordered form in which any hydrogen bonds are randomly disposed and are not the specifically directed bonds of the double helix. These conclusions are confirmed by the ultraviolet absorption of the nucleate after various titration cycles.

The mechanism suggested by these results has been used to analyse earlier observations on the effect of changes in temperature and in ionic strength on the relation between the forward- and the back-titration curves both above and below pH 7. The energy relations between the various forms of the deoxyribonucleate molecule and related problems are also discussed.

The hydrogen bonds cross-linking the two helical polynucleotide chains of sodium nucleate may be irreversibly ruptured by heat,[1] ionising radiation,[2] acid, or alkali,[3,4] and the proportion of hydrogen bonds destroyed by these agents may be computed[1] from the relative positions of the forward- and the back-titration curves obtained on subsequent titration. The irreversible rupture of hydrogen bonds (" denaturation ") during forward-titration from neutrality with acid or alkali has not hitherto been examined closely, although certain features of the effects of ionic strength[5] and of temperature[6] on the forward-titration curves have suggested that it may not always be necessary to ionise all the hydrogen-bonded amino-groups in order to attain complete denaturation and that the ease of denaturation by acid increases with temperature. Two limiting forms of behaviour have also been observed: complete ionisation without denaturation[6,7] at low temperature and, conversely, complete denaturation[1] by heat without change of pH.

We now report a more detailed study of acid denaturation made by first lowering the pH to various points intermediate between neutrality and the pH of complete denaturation and then back-titrating the solution with alkali. The relative positions of the curves obtained in this way must depend on the course of denaturation as a function of pH and should be informative about the mechanism of acid denaturation. Parallel ultraviolet-absorption measurements have also been made since the intact double-helical structure appears to have an especially low extinction which increases irreversibly on denaturation.[8,9]

Experimental

The preparation and characteristics of the herring-sperm sodium deoxyribonucleate used have been given elsewhere.[5]

* Part V, *J.*, 1957, 4724.

[1] Cox and Peacocke, *J.*, 1956, 2646.
[2] Cox, Overend, Peacocke, and Wilson, *Nature*, 1955, **176**, 919.
[3] Gulland, Jordan, and Taylor, *J.*, 1947, 1131.
[4] Lee and Peacocke, *J.*, 1951, 3361.
[5] Cox and Peacocke, *J.*, 1956, 2499.
[6] *Idem*, *J.*, 1957, 4724.
[7] Preston and Peacocke, unpublished work; Peacocke, *Chem. Soc. Special Publ.*, No. 8, 1957, p. 161.
[8] Laland, Lee, Overend, and Peacocke, *Biochim. Biophys. Acta*, 1954, **14**, 356.
[9] Thomas, *ibid.*, p. 231.

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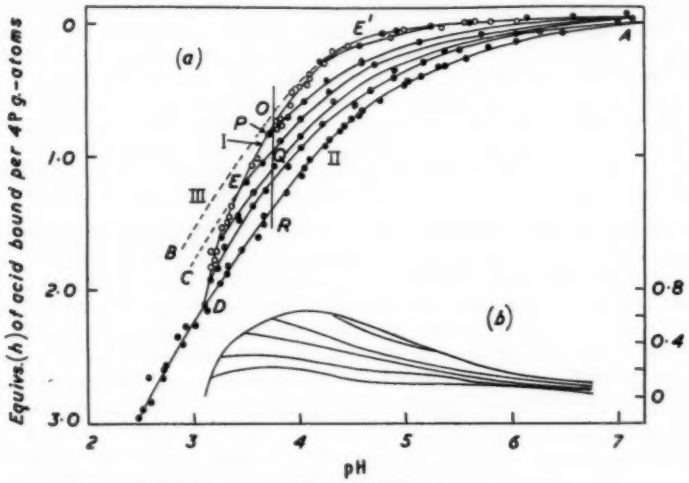
Solutions of sodium nucleate (0·2% in 0·05M-sodium chloride) were titrated electrometrically in cells with liquid junctions by a continuous method, as described previously.[5] 0·1N-Hydrochloric acid was added in 0·0002 ml. portions to solutions well stirred by a stream of nitrogen, until the required pH (between 3·1 and 7) was attained. Alkali was then added in a similar manner to pH 10.

Titration curves are shown as the corrected number (h) of equivalents of acid (*i.e.*, hydrogen ions) bound by an amount of the nucleate containing 4 P g.-atoms as a function of pH on a standard scale [10] on which 0·05M-potassium hydrogen phthalate has a pH of $4{\cdot}00_5$ at 25°.

The ultraviolet absorption values of the various acid-treated nucleate solutions (pH 7·5, in 0·05M-sodium chloride), after dilution with 0·05M-sodium chloride and centrifugation (45 min., 5000 r.p.m.), were measured against 0·05M-sodium chloride with a Unicam spectrophotometer. The extinction coefficients of several independent dilutions of the same stock solution agreed within 1%.

FIG. 1. (*a*) *Titration curves of herring-sperm sodium deoxyribonucleate at* 25° *in* 0·05M-*sodium chloride solution: the effect of graded acid treatment.*



I, *Irreversible forward-titration curve with acid* (*APED*).
II, *Reversible back-titration curve with alkali from D or lower* pH (*DRA*).
III, *Reversible titration curve of the intact* DNA *structure* (*AE'OB*).
EQA, Reversible back-titration curve with alkali from E (*similarly for the other intermediate curves*).
(*b*) (*Lower figure*), *Difference curves. Ordinate scale* (*lower right*) *represents the acid bound along curve DRA* minus *the acid bound along the various intermediate curves, such as AQED.*

Results.—The continuous titration curves at 25° in 0·05M-sodium chloride are shown in Fig. 1. Curve I is the usual irreversible forward-titration curve for the sodium nucleate and points obtained by many independent titrations all fall accurately on it; curve II is the reversible back-titration curve and there is substantial evidence [1] that it represents the dissociation curve of non-hydrogen-bonded nucleate. The curves intermediate between I and II were obtained by back-titration from various pH's higher than the point (*D*) of intersection of I and II. The forward-titration curve was reversible between pH 4·55 and pH 7·00, and the curve obtained on back-titration from pH 4·20 was little different from curve I. This implies that at 25° all of the first 10% and most of the first 18% of the hydrogen-bonded amino-groups that are titratable gain and lose protons reversibly.

At pH's less than 4·20 the difference between the forward- and the back-titration curves is marked and the curves shown between I and II (Fig. 1) must correspond to mixtures of hydrogen-bonded and non-hydrogen-bonded nucleate.[1, 11] The steep gradient of the forward-titration curve over the range pH 4·25—3·10 particularly between pH 3·10 and 3·15 shows

[10] British Standard 1647: 1950.
[11] Cox and Peacocke, *J. Polymer Sci.*, 1957, **23**, 765.

that larger irreversible changes in hydrogen-bonding in the nucleate are brought about by very small changes in pH in this region.

The curves intermediate between I and II were shown to be reversible in the following way. Nucleate was titrated with acid to pH 3·50 (*E*) and the curve (*EQA*) was followed on back-titration with alkali to neutrality (*A*). The curve for the subsequent re-titration with acid from *A* was identical with *EQA* over the range pH 7·00—3·50 down to *E* and followed I between this point and pH 3·10 (*D*). Curve II was followed on back-titration with alkali from pH 3·10 (*DRA*). Thus the partly denatured nucleate, whose pH had previously been reduced to *E* and then increased to *A*, had the forward-titration curve *AQED* with acid and on back-titration with alkali from *D* gave the usual curve II. Fig. 1(*b*) is a plot of the difference in acid bound between *AQED* and *DRA* (II) for varying positions of the reversal point *E*, and thus for nucleate samples denatured by acid to various graded extents.

Although the initial titration with acid at 25° resulted in irreversible changes in the nucleate the pH was always stable for at least 30 min. after the addition of acid, and the forward-titration curves were accurately reproducible. Thus any further denaturation that may have followed the first rapid opening up of the hydrogen bonds must have proceeded too slowly to affect the titration behaviour of the nucleate partly denatured with acid. Denaturation by alkali has similarly been shown [12] to take place instantaneously since the pH during forward-titration with alkali has been reported as stable for at least 18 hr.

The ultraviolet absorption at λ 200—300 mμ of nucleate solutions which had undergone the various titration cycles was measured at pH 7·5 in 0·05M-sodium chloride. An increase in absorption compared with the original nucleate was observed in all cases where acid treatment resulted in a difference between the forward- and the back-titration curves, *i.e.*, when denaturation occurred. This increase, represented as a percentage of the maximum attainable, is shown in Fig. 2(*a*) as a function of the fraction (γ) of the groups originally involved in hydrogen bridges which were *ionised* at the reversal point (*P*,*E*, etc.) of the titration cycle that each nucleate solution had previously undergone. At $\gamma > 0{\cdot}1$ the relation is linear and the maximum increase in absorption (14% of the original absorption at λ 260 mμ) was attained when $\gamma = 0{\cdot}75$; from all previous evidence,[1,8] this maximum corresponds to complete breakdown of the hydrogen-bonded structure. The dependence of the increase in ultraviolet absorption on the fraction (β) of the original specific hydrogen bonds which have been *permanently ruptured* is also shown, in Fig. 2(*b*), and is discussed below, where it is shown that β and γ are not necessarily equal since ionisation can occur without the hydrogen bonds' being permanently broken.

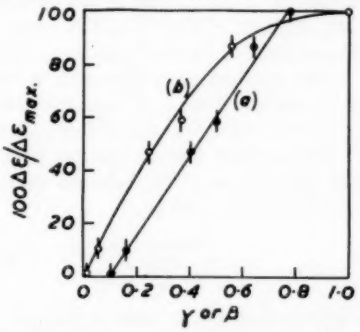


FIG. 2. *The effect of graded acid treatment at 25° on the ultraviolet absorption of sodium deoxyribonucleate at λ 260 mμ.*

Ordinate: Increase in absorption ($\Delta\varepsilon$) *represented as a percentage of the maximum increase* ($\Delta\varepsilon_{max.}$) *attained. Abscissa: For curve* (*a*), *the fraction* (γ) *of groups originally involved in hydrogen bonds which were ionised at reversal point* (*P*, *E*, *etc.*, Fig. 1) *of the titration cycle. For curve* (*b*), *the fraction* (β) *of the original hydrogen bonds which have been permanently ruptured by the titration cycle* (*for calculation, see text*).

Discussion

There is now considerable evidence that the nucleate ion retains the double-helical configuration of the solid state when dissolved in neutral salt solutions and that, at 25°, this configuration may be lost on treatment with acid, *e.g.*, to pH 3·10 in 0·05M-sodium chloride. The " anomalous " titration curve of the nucleate may then be attributed to the irreversible rupture of the complementary hydrogen bonds which bridge the two helices and to the loss of the double-helical structure, a process designated as " denaturation " in this discussion. The results reported above show that the pH may be lowered

[12] Shack and Thompsett, *J. Biol. Chem.*, 1952, **197**, 17.

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to 4·5 (E') without the occurrence of any irreversible change. The number of groups ionised at this pH corresponds to about 10% of those amino-groups which were originally involved in hydrogen bridges at neutrality. Thus above pH 4·5 the ionisation of an amino-group and the consequent disappearance of the hydrogen bridge is not sufficient to cause a permanent change in configuration. The reversible dissociations occurring over this pH range may be represented as:

$$\underset{(a)}{\{\text{Helix}\}\text{–NH}_3^+ + (\text{–NH·CO–})\{\text{Helix}\}} \rightleftharpoons \underset{(b)}{\{\text{Helix}\}\text{–NH}_2 \ldots (\text{–NH·CO–})\{\text{Helix}\} + \text{H}^+} \quad \ldots \quad (1)$$

where –NH_3^+ and –NH_2 are the charged and the uncharged form of the 1 : 6-amino-system capable of being hydrogen-bonded (adenine and cytosine 6-amino-groups [13] and, possibly,[14] the guanine 2-amino-group), (–NH·CO–) is the system to which these groups are hydrogen-bonded in the double helix (the 1 : 6–NH·CO– systems of thymine and guanine [13] and, possibly,[14] the cytosine 2-oxo-group); the terms enclosed in braces represent the configuration of the polynucleotide chains and the dotted line represents a hydrogen bond * of the complementary type.[13] At lower temperatures (below −0·4°) the dissociations appear to be of this type over the whole pH range and the double helical configuration is presumed to be retained.[7] The reversible forward-titration curve of nucleate in the double-helical form at −0·4° has recently been observed directly [7] and was first inferred [6] from the curves at +0·4°; from it the reversible forward-titration curve at 25° may be deduced (III, *AE'OB*, of Fig. 1) and is, in fact, almost identical with it because of the low heats of dissociation of the 6-amino-groups of adenine and cytosine.[6]

The appearance and growth of the titration anomaly at 25°, as the pH at the reversal point became more acid than 4·5, indicates the onset and increasing extent of denaturation, which was complete at pH 3·10, all the 6-amino-groups of adenine and cytosine and some of the guanine 2-amino-groups being then ionised. On back-titration with alkali from pH 3·10 or lower, dissociation of the denatured nucleate (curve II) was reversible and may be represented as:

$$\underset{(c)}{\left\{\begin{matrix}\text{Denatured}\\ \text{chain}\end{matrix}\right\}\text{–NH}_3^+ + \text{H}_2\text{O}} \rightleftharpoons \underset{(d)}{\left\{\begin{matrix}\text{Denatured}\\ \text{chain}\end{matrix}\right\}\text{–NH}_2 \ldots (\text{H}_2\text{O}) + \text{H}^+} \quad \ldots \quad (2)$$

The notation is the same as for (1) except that the dotted lines now represent hydrogen bonds of a non-specific type involving solvent molecules. The dissociation curve for a mixture of the two forms should be intermediate between I and II at a position determined by its composition. If R and O are, respectively, points at a given pH on the reversible titration curves (II, III) shown in Fig. 1 for denatured and undenatured nucleate and if Q is a point on the (reversible) curve for a mixture containing a fraction β of the nucleate in the denatured form (measured as nucleotide units), then, by a previous argument,[1] $\beta = OQ/OR$. Values of β deduced in this way from the intermediate back-titration curves † (*e.g.*, *EQA* of Fig. 1) are given in Table 1 and, over the pH range in which it can be calculated, β was reasonably independent of pH. Thus β may be obtained for any point P on the usual forward-titration curve from a *single* calculation of OP/OR for that point, and hence the variation of β with the number of groups ionized over the whole of the forward-titration can be deduced.

A point on the forward-titration curve, which corresponds to an extent of denaturation β, must also be a point on the titration curve for (1 − β) mole of undenatured and β mole of denatured sodium nucleate. Thus the point E at pH 3·50 lies on the curve *CEQA*

* Here, and in what follows, the term hydrogen " bond " or " bridge " in the singular will refer, unless otherwise indicated, to the two (or three) such bonds regarded as linking a pair of bases, one in each helical polynucleotide chain.

† The reversibility of these curves shows that there is no denaturation as a result of high local concentrations of acid or alkali when these reagents are added.

[13] Watson and Crick, *Nature*, 1953, **171**, 737.

[14] Pauling and Corey, *Arch. Biochem. Biophys.*, 1956, **65**, 164.

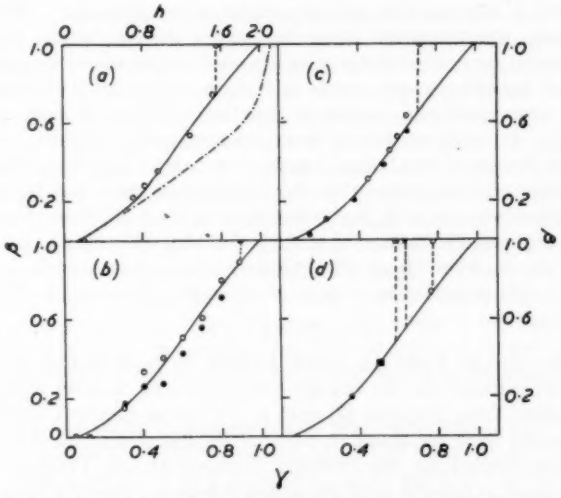
TABLE 1. *The extent of denaturation (β) deduced at various points on the intermediate back-titration curves of Fig. 1.*

Back-titration curves from the reversal points		β * at points on these curves								Average
h	pH	pH: 3·25	3·50	3·75	4·00	4·25	4·50	4·75	5·00	β
0·84	3·75	—	—	0·17	0·20	0·22	0·22	0·22	0·25	0·22
1·20	3·48	—	0·27	0·34	0·34	0·38	0·38	0·36	0·38	0·35
1·62	3·25	0·55	0·49	0·49	0·51	0·50	0·58	0·56	0·62	0·53
1·94	3·15	0·70	0·65	0·68	0·72	0·74	0·80	0·76	0·71	0·73

* *E.g.*, at the point *Q* on *EQA* of Fig. 1, $\beta = OQ/OR$ (see main text).

(Fig. 1) for which $\beta = 0{\cdot}35$. Only the portion *EQA* of this curve is experimentally accessible, since when the pH is decreased by a small amount (δpH) from pH 3·50 the

FIG. 3. *The dependence of the fraction (β) of hydrogen bonds permanently ruptured on the fraction (γ) of 6-amino (or 1 : 6-NH·CO⁻)-groups ionised during titration. Ordinate, β; lower abscissae, γ. In (a)—(d) the full line is the theoretical curve for β–γ on the assumption that n = 2 in equation (3) (see text).*



(*a*) ○, *Points derived for β–γ from the forward-titration curve with acid at 25° in* 0·05M-NaCl (*APED*, Fig. 1).
— · — · — *curve of β against the number (h) of protons bound per* 4P *g.-atoms (abscissa at the top of the diagram).*

(*b*) *β as a function of the fraction of* 1 : 6-NH–CO⁻ *groups ionised on forward-titration with alkali* [5] *at 25°.*
○, *In* 0·05M-NaCl; ●, *in* 0·50M-NaCl.

(*c*) *The effect of temperature* [6] *on denaturation occurring during titration with acid in the presence of* 0·05M-NaCl.
○, *Deduced from titration at* 35°; ●, *deduced from titration at* 0·4° (*precipitation occurred at* $\gamma = 0{\cdot}65$).

(*d*) *The effect of ionic strength* [5] *on denaturation during titration with acid at 25°; for simplicity only the values of β when γ = 1 are shown except at high ionic strengths where precipitation intervened before denaturation was complete.*
□, *Titration in the absence of added salt. Titration at ionic strengths of:* × 0·02; ○ 0·05; ■ 0·15; ● 0·50.
At the last two ionic strengths the nucleate was precipitated from solution at values of γ higher than those indicated.

fraction of denatured regions immediately increases to $(\beta + \delta\beta)$ and it is the curve for a mixture of denatured and undenatured nucleate in the ratio $(\beta + \delta\beta)$ to $[1 - (\beta + \delta\beta)]$ which is then followed on back-titration from pH (3·50 − δpH). The forward-titration curve therefore represents a transition from the curve for $\beta = 0$ to that for $\beta = 1$ by way of a continuous series of curves of the type *CEQA*, each representing a more denatured

molecule than the previous one until the double-helical structure is completely destroyed ($\beta = 1$). This transition is shown in Fig. 3(*a*) where β is given as a function of h, which is proportional to the number of hydrogen ions bound. However, h is compounded both of the ionisations of groups originally hydrogen-bonded (6-amino-groups) and of the protons bound by groups not originally hydrogen-bonded, such as primary phosphate groups and, possibly, the guanine 2-amino-groups.* At various pH's the contribution to h of these last two groups was estimated from their pK'_a values and from the titration curves of reduced apurinic acid,[15] so that the fraction (γ) of 6-amino-groups ionised at a given pH was derived. In Fig. 3(*a*) the fraction (β) of hydrogen bonds permanently destroyed is also shown as a function of γ: the curves indicate that the first few ionisations ($\gamma < 0{\cdot}1$) had little effect on the double-helical configuration but that denaturation increased rapidly as the hydrogen-bonded groups became charged until 75% of them were ionised. At this critical point ($\gamma = \gamma_c$) the remaining hydrogen bonds were broken without further ionisation.

This behaviour is consistent with the idea [1,11,16] that co-operative rupture of a number of hydrogen bonds is necessary to ensure permanent denaturation. Since the hydrogen bonds succeed each other regularly along the axis of the two helices, it is reasonable to suppose that a necessary condition for a region of the molecule to be denatured is that a minimum number (n) of hydrogen bonds in sequence must all be ruptured at one time. The number n represents the minimum length of polynucleotide chain which can sufficiently change its configuration by rotation about the covalent bonds of the main chain so that the chance of the helical form's ever being regained is infinitesimal.

It has previously been suggested that the acid-denaturation may be explained in these terms and a relation between n, β, and γ has been derived in terms of a statistical model which assumes a random distribution of protons and that all breaks are equally probable.[11] On this model, the fraction (β) of all hydrogen bonds permanently lost, which is the fraction of such bonds occurring as sequences of length n or more, is: [11]

$$\beta = \gamma^n[n + \gamma(1 - n)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where γ is the fraction of hydrogen bonds broken by random ionisation, *i.e.*, it is the probability at that instant that the linkage between a pair of bases will be severed. The values of β calculated from equation (3) with $n = 2$ are in excellent agreement with those found experimentally over the range $\gamma = 0 - 0{\cdot}75$ [Fig. 3(*a*)]. If the guanine 2-amino-group is hydrogen-bonded to the cytosine 2-oxo-group, as Pauling and Corey have suggested,[14] and stays so bonded until the group is ionised, then the value of γ for a given β will be not more than 10% higher than is indicated by the open circles of Fig. 3(*a*). The value of n would then be a little larger than 2 although comparison of the curve of β as a function of the total number of amino-groups ionised with the family of β–γ curves [11] for various n shows that $n \not> 3{\cdot}0$. However, as has been pointed out elsewhere,[17] it is improbable that a single hydrogen bond on the guanine 2-amino-group would continue to link it with cytosine once the two hydrogen bonds at the respective 1 : 6-positions had disappeared by ionisation of the cytosine 6-amino-group at low h values ($0 - 0{\cdot}5$). Thus, on the present evidence, it appears more reasonable to assume that the guanine 2-amino-group is no longer hydrogen-bonded when the pH is low enough for it to ionise ($h \gg 0{\cdot}1$), whatever its state in the original double-helix may have been. This would be consistent with the observed [5] coincidence of the back-titration curve from pH 2·6 with that from pH 12, at which pH only the hydrogen bonds to the 1 : 6-position of guanine can be directly ruptured by ionisation. A value of 2 for n therefore seems the most likely in the

* Or, equivalently, if these groups are hydrogen-bonded in the original nucleate, they have lost their hydrogen bonds as a result of the rupture of hydrogen bonds at the guanine 1 : 6-position through ionisation of the cytosine 6-amino-group.

[15] Hurlen, Laland, Cox, and Peacocke, *Acta Chem. Scand.*, 1956, **10**, 793.
[16] Doty, Proc. 3rd Congr. Biochem., Brussels, Academic Press, New York, 1955, p. 135.
[17] Peacocke, *Chem. Soc. Special Publ.*, No. 8, p. 139.

present instance and is supported by the agreement obtained under other conditions of temperature and ionic strength (see below). The most important departure from the curve of equation (3) with $n = 2$ is the sudden transition from $\beta = 0{\cdot}75$ to $1{\cdot}0$ at a critical value, $\gamma_c = 0{\cdot}75$. It thus appears that when only 25% of the total number of hydrogen bonds are left the structure becomes unstable and the remaining bonds and helical regions become rapidly disorganised to the completely denatured form. This type of process is sometimes described as a " zipper-like " action since the 25% of the groups which are suddenly released from hydrogen bonds are not at this point ionised: they are ruptured apparently because the entire structure suddenly becomes unstable at this point.

Cavalieri and Rosenberg [18] have put forward a different view of the process of acid-denaturation which attributes it mainly to the ionisation of the guanine 2-amino-groups. This was originally propounded [18b] partly to explain the supposed difference between the reversible curves obtained on back-titration from pH 2·6 and pH 12, but since these have now been shown [5] to be coincident this particular argument cannot apply. This view was also based [18b] on their observation that the forward-titration curve was reversible up to the very steep part, " the point of inflection," where nearly all the cytosine and about half of the adenine 6-amino-groups were considered [18b] to be ionised. Thereafter it became irreversible. This contrasts with the observations recorded in Fig. 1, which shows reversibility only in the first 10—20% of these ionisations. Unfortunately these authors have not published detailed curves and points, so that the necessary detailed comparison between the two sets of observations cannot yet be made. It seems difficult, on their view, to explain the observations at 35° (ref. 6) and at 37° and 63° (ref. 18*a*) which show that the point (D) of coincidence of the forward- and the back-titration curves moves with increasing temperature to higher pH and lower h values, where few ionisations of the guanine 2-amino-group can be occurring. (Similar remarks apply to titrations at 25° in the absence of salt.) Their explanation of this observation then has to be based on prior denaturation by heat which is unlikely at these temperatures (see below). For these reasons, the acid-denaturation phenomenon is here attributed to the ionisation of all amino-groups originally involved in hydrogen bonds and not especially to that of the guanine 2-amino-group.

The changes in the ultraviolet absorption of neutral nucleate solutions (25°; ionic strength = 0·05) after titration cycles to various pH values and back are shown in Fig. 2(*b*) as a function of β, deduced as already described. The curve is slightly concave to the β axis and this is not surprising since the cytosine 6-amino-groups are presumably ionised before the adenine 6-amino-groups as the pH is lowered and rupture of these two different types of group may lead to different changes in absorption. The maximum increase in absorption is attained at $\beta \sim 0{\cdot}7$—$0{\cdot}8$, rather before the point of complete denaturation ($\beta = 1$). This suggests that when the critical extent of denaturation ($\beta = 0{\cdot}75$) and degree of ionisation ($\gamma_c = 0{\cdot}75$) are reached the molecules are already sufficiently disorganised to have an ultraviolet absorption very little different from that of the completely denatured state at $\beta = 1$.

The transition from $\beta = 0$ to $\beta = 1$ with ionisation also occurs on treatment of nucleate with alkali since the same reversible back-titration curve is ultimately obtained as for acid-treatment.[5] Calculations on the more limited data available on the forward titration with alkali show [Fig. 3(*b*)] that also in this case complete denaturation ($\beta = 1$) occurs before ionisation of all the hydrogen-bonded groups (*viz.*, at $\gamma_c = 0{\cdot}9$). Up to this point, the plot of β against γ, which now represents the $^-NH{\cdot}CO^-$ ionisation, again follows the curve of equation (3) with $n = 2$, although the points are less reliable because of their more indirect derivation.

In previous publications the effects of changes in temperature [6] and ionic strength [5]

[18] Cavalieri and Rosenberg, (*a*) *J. Amer. Chem. Soc.*, 1957, **79**, 5352; (*b*) *Biochim. Biophys. Acta*, 1956, **21**, 202.

on the titration curves of the nucleate were reported. The effects on the forward-titration curves may now be examined with reference to the preceding analysis.

Effect of Temperature.—The effect on sodium deoxyribonucleate of treatment with acid to low pH varies with temperature: at −0·75° all groups are ionised reversibly and there is no denaturation; [7] at 0·4° about 40% denaturation occurs; [6] and at 25° and higher temperatures the maximum degree of denaturation [6] is attained. Heating at pH values close to neutrality causes complete denaturation only at temperatures of 75° or higher [1,16] (according to the sample). Below this critical temperature no denaturation has been observed, which renders improbable Cavalieri and Rosenberg's view [18a] that the displacement [6,18a] of the point D to higher pH values with increasing temperatures in the range up to 63° can be explained by rupture of hydrogen bonds by heat *before* titration. An alternative interpretation of this displacement of the point (D) of coincidence of forward- and back-titration curves is developed below after analysis of the forward-titration curves.

The fraction (γ) of groups, originally hydrogen-bonded, which are ionised at various points on the forward-titration curves at 0·4° and 35° may be computed as for the 25° curves: the pK'_a of the primary phosphoryl groups and the 2-amino-groups of guanine at 0·40° and 35° were estimated from the 25° data by assuming [6] apparent heats of dissociation of zero and 4 kcal./mole, respectively. Values of β were computed for the same points on these curves by the methods described above and are plotted as a function of γ in Fig. 3(*c*). The points again lie on the curve of equation (3) with $n = 2$ and are therefore consistent with co-operative rupture of two adjacent hydrogen bonds. As at 25°, when γ exceeds a critical value (*viz.*, 0·7) at 35° the remaining specific hydrogen bonds and helical regions suddenly break down and all the groups involved change to a state in which their dissociation constants are those of the denatured configuration. This critical value (γ_c) decreases with increasing temperature [cf. Figs. 3(*a*), 3(*c*)] and above a certain temperature (*ca.* 75° for this sample) the molecule can be completely denatured even at neutral pH. The increasing instability of the double-helical structure with rising temperature is therefore manifested in a lowering of γ_c and this appears to be sufficient explanation of the upward displacement of the point D at higher temperatures. At 0·4° γ_c was never attained [1,11] and this is attributed to the *increased* contribution to the observed h of the 2-amino-group of guanine at low temperatures, owing to differences in the temperature coefficients of the pK'_a's of the various amino-groups. (This is further evidence against any special rôle of the guanine 2-amino-group in initiating acid denaturation).

TABLE 2. *Free-energy relations in the dissociations in the forward- and the back-titration curves.*

Ionic strength (μ)	0	0·02	0·05	0·15	0·50
Acid branch ($h>0$)					
† $(\Delta pH)_{h=0}$	0·4	0·8	1·4	1·7	1·7
$(\Delta G_2^\circ - \Delta G_1^\circ)$ (kcal./mole)	0·5	1·1	1·9	2·3	2·3
Alkaline branch ($h<0$)					
†$(\Delta pH)_{h=0}$	—	−1·0	−1·1	−1·2	−1·2
$(\Delta G_4^\circ - \Delta G_3^\circ)$ (kcal./mole)	—	−1·4	−1·5	−1·6	−1·6

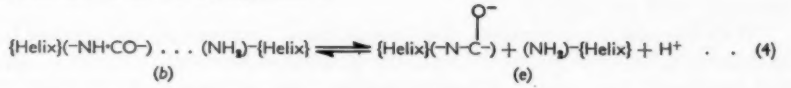
† $(\Delta pH)_{h=0}$ = limiting value of ΔpH as $h \longrightarrow 0$, where $(\Delta pH)_h = (pH_{back} - pH_{forward})_h$ at a given h and is obtained from the 25° curves of Figs. 1—4 (ref. 5).

Effect of Ionic Strength (μ).—It was earlier observed [5] that, at given values of h, both the difference in pH between the forward- and the back-titration curves and the value of h at the point (D of Fig. 1) where these curves meet increase as the concentration of sodium chloride increases. At 25°, when $0 < h < 0{\cdot}3$, and both the forward- and the back-titration curves are reversible (see above), the difference in pH between them at a given h is the positive quantity $(\Delta pH)_h = (pH_{back} - pH_{forward})_h = (pH_2 - pH_1)_h = (pK'_2 - pK'_1)$, where subscripts 1 and 3 refer to the reversible dissociations of the helical and the denatured form, as in equations 1 and 2 and curves III and II (Fig. 1), respectively;

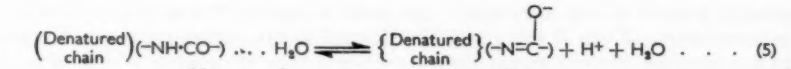
K'_1 and K'_2 are the apparent acidic dissociation constants. Since the corresponding apparent standard free energies of dissociation, $\Delta G°$, are given by $\Delta G° = \boldsymbol{R}T \ln K' = 2{\cdot}303\boldsymbol{R}T \,.\, pK'$, it follows that $(\Delta pH)_h = (\Delta G_2° - \Delta G_1°)/2{\cdot}303\,\boldsymbol{R}T$. Values of (ΔpH) and of $(\Delta G_2° - \Delta G_1°)$ as h approaches zero from positive values have been deduced from the curves previously obtained [5] at various ionic strengths (Table 2); the factors contributing to this free-energy difference are discussed in the Appendix.

Plots of β against γ [Fig. 3(*d*)] were derived by the methods outlined above from the forward-titration curves with acid at 25° for the reversal points at different ionic strengths [5] and proved to be similar to those of Figs. 3(*a*) and 3(*c*); a similar mechanism apparently applies with n again equal to 2. The values of γ_c at 25° are calculated to be 0·58 in the absence of added salt and 0·69 at $\mu = 0{\cdot}02$ (cf. $\gamma_c = 0{\cdot}75$ at $\mu = 0{\cdot}05$) (complete denaturation was not attained in forward titration at ionic strengths of 0·15 and 0·50 because of precipitation of the nucleate [4]).

For the alkaline branches of the titration curves ($h < 0$), in which hydrogen ions are being *removed* during the forward titration, $(\Delta pH)_h$ may also be obtained and is here a negative quantity equal to $(\Delta G_5° - \Delta G_4°)/2{\cdot}303\,\boldsymbol{R}T$. The quantities $\Delta G_4°$ and $\Delta G_5°$ are the apparent standard free energies of dissociation of the helical and the denatured form when involved in the following equilibria:



(4)



(5)

Here (–NH·CO–) and (–N=C–) represent the un-ionised and the ionised systems at the 1 : 6-positions of thymine and guanine, and $-NH_2$ represents the amino-group to which these systems are hydrogen-bonded in the double helix; other symbols are as in equations (1) and (2). [Note that because the complementary hydrogen bonds link the two types of dissociable group, forms (*b*) and (*d*) of equations (1) and (2) also appear in equations (5) and (6). The free-energy differences in the alkali and the acid branch of the curves are compared in the Appendix.] The values for $(\Delta pH)_h$ and $(\Delta G_5° - \Delta G_4°)$ are given in Table 2. In summary, it may be said that the critical degree of ionisation (γ_c) when the partly denatured molecule suddenly breaks down decreases on increase of temperature and on decrease of ionic stength: and that, apart from the direct effects of temperature and ionic strength on the pK'_a of the ionising groups, it is changes in γ_c which appear to be chiefly responsible for the altered shapes of the forward-titration curves relative to the back-titration curves.

The energy relations of the various forms (*a*)—(*d*) that are involved in titration with acid present an interesting problem. Let $G°$ with appropriate subscripts represent the free energy of these various forms under standard conditions. At 25°, $\Delta G_1°$ and $\Delta G_2°$ are both positive, so that $G_b° > G_a°$ and $G_d° > G_c°$; moreover $\Delta G_1° > \Delta G_2°$ (Table 2) and $(G_d° - G_b°)$ is probably positive (see Appendix). Thus the order of decreasing free energies at 25° in the standard state (unit activity in solution) appears to be $d > b > a, c$. At higher temperatures, *e.g.*, 100°, there is evidence [19] that $G_b° > G_d°$, so that (*d*) and (*b*) would have to be interchanged.

The relative free energies of the ionised helical and the denatured form, (*a*) and (*c*), show some interesting features. The $G°$ terms represent the free energies in the standard state per mole of ionisable groups, *i.e.*, per mole of hydrogen-bonded base pairs (one

[19] Rice and Doty, *J. Amer. Chem. Soc.*, 1957, **79**, 3937.

proton-accepting group being assumed per hydrogen-bonding system). The earlier analysis has suggested that when two adjacent groups in the double helix are ionised and cease to be hydrogen-bonded then the helical configuration is permanently lost and the polynucleotide chain takes up its random configuration (*c*) in that region. This means that instead of the free energy of two adjacent ionised groups in the helical structure being $2G_a^\circ$, as for two isolated ionisations, it now becomes $G_c^\circ = (2G_a^\circ + \Delta G^\circ_{\text{config.}})$, where $\Delta G^\circ_{\text{config.}}$ is the change in free energy consequent upon the extra configurational freedom of the random chain in state (*c*). Since $\Delta H_{\text{config.}}$ will be negligible, no new bonds being formed or broken in the change (*a*) to (*c*), and $\Delta S_{\text{config.}}$ will be positive owing to the loss of order, $\Delta G_{\text{config.}}$ $(= \Delta H_{\text{config.}} - T.\Delta S_{\text{config.}})$ will be a negative quantity, and $G_a^\circ - G_c^\circ = -\Delta G_{\text{config.}}/2$. Thus the free-energy sequence can be tentatively deduced as $d > b > a > c$ at 25° and at other temperatures (below the critical denaturation point) where the β–γ relation is determined by $n = 2$ in equation (3). At these temperatures, the critical point in ionisation ($\gamma = \gamma_c$) presumably corresponds to a point where the *average* energy per base pair has been so enhanced by the extra rotational (etc.) energy of movement in the undenatured regions that it reaches, as it were, the critical " temperature " and the remaining hydrogen bonds between un-ionised groups break down. (This interpretation assumes that denatured and helical regions co-exist in the same molecule; but see below.)

With increase in temperature, the " equilibrium " between (*b*) and (*d*) may be regarded as shifting in favour of (*d*), according to the evidence of Rice and Doty [19] (*i.e.*, ΔH positive), and eventually $G_d^\circ < G_b^\circ$. The denaturation then appears to be thermal and not to involve ionised forms, although it has been suggested [20] that these are still necessary intermediates. Even if this is so, the thermal denaturation process is much more akin to the situation in the forward titration when $\gamma \geqslant \gamma_c$ than when $\gamma < \gamma_c$ where the $n = 2$ mechanism applies. Thus this latter mechanism need not be opposed to that thought [1,11,16] to prevail in purely thermal denaturation when longer sequences (10—100) of hydrogen bonds are regarded as being broken simultaneously. However, much more quantitative information is necessary on thermal denaturation before any detailed comparison can be properly made.

Most observers agree that the acid-denaturation process occurs extremely quickly and apparently coincidentally with ionisation.* The " free energy " of activation involved in the process (*a*) ⟶ (*c*) must therefore be very small and beyond the range of present methods of study. Again, this seems to be different from thermal denaturation for which small but finite " free energies " of activation, coupled with large heats and entropies of activation, have been provisionally deduced.[1,19,21]

In the foregoing, it has been tacitly assumed that the original double-helical molecule can be partly denatured so that double-helical (" crystalline ") regions and denatured disordered (" amorphous ") regions are juxtaposed within any one molecule (*e.g.*, ref. 17, Fig. 6, but with $n = 2$). It has however been suggested [22] that in the partially denatured state ($0 < \beta < 1$) some of the molecules are completely denatured and the rest remain intact. This may well be so after denaturation by heat, when the rupture of a fairly long sequence of hydrogen bonds seems to be the essential step and could then reasonably be expected to result in a complete breakdown of the rest of the molecule. However, the process of denaturation by ionisation differs from this in certain respects, notably in the character of the difference curves.[11] In particular, the agreement of the deduced β–γ

* The rapidity of acid-denaturation to a β value which then remains stable suggests that in the intact regions the continual interchange of protons scarcely ever produces new disordered sequences or, if so, only extremely slowly. This stability is not inconsistent with the titration curves of the helical structure, when allowance is made for the guanine ionisation, and may also be enhanced by unfavoured sequences of the bases in the remaining intact regions (see discussion in ref. 11, p. 776).

[20] Cavalieri, Rosoff, and Rosenberg, *J. Amer. Chem. Soc.*, 1956, **78**, 5239.
[21] Dekker and Schachman, *Pro. Nat. Acad. Sci. U.S.A.*, 1954, **40**, 894.
[22] Doty, comments on a paper by Peacocke and Preston, *J. Polymer Sci.*, 1958, **31**, 1.

plots with equation (3) for $n = 2$ is more consistent with partial denaturation within each molecule, on which equation (3) was based,[11] than with the alternative "all-or-nothing" possibility.

Appendix

The quantity $(\Delta G_2^\circ - \Delta G_1^\circ)$ has been discussed * in the preceding paper of this series,[6] where it was suggested that it can be regarded as the sum of a non-electrostatic term, independent of ionic strength (μ), and an "electrostatic" term which varies with μ. If subscripts (*a*)—(*d*) denote the same molecular species as in equations (1), (2), (4), and (5), and subscripts ν and μ the terms independent of and dependent upon μ, then

$$(\Delta G_2^\circ - \Delta G_1^\circ) = (G_d^\circ - G_c^\circ) - (G_b^\circ - G_a^\circ) =$$
$$[(G_a^\circ - G_c^\circ)_\nu + (G_d^\circ - G_b^\circ)_\nu] + [(G_a^\circ - G_c^\circ)_\mu + (G_d^\circ - G_b^\circ)_\mu] \quad . \quad . \quad (6)$$

where the G° are free energies under standard conditions, each equal to $[(G^\circ)_\nu + (G^\circ)_\mu]$.

At high μ the effects of interionic forces are minimal, so that a decrease of μ from 0·50 to 0·02 should increase the influence of the "electrostatic" factors and was observed to diminish $(\Delta G_2^\circ - \Delta G_1^\circ)$ by 1·8 kcal./mole, which means that it reduces the acidity of the helical form relative to that of the denatured state. The parallel displacement of the back-titration curves [5] with changing μ has already indicated [23] that the electrostatic potential at the amino-groups is determined by its immediate environment and depends very little on the configuration of the polynucleotide chain configuration, so that $(G_a^\circ - G_c^\circ)_\mu$ should be negligible. Hence the decrease in $(\Delta G_2^\circ - \Delta G_1^\circ)$ with decreasing μ must be attributed mainly to a decrease in $(G_d^\circ - G_b^\circ)_\mu$, which means that the free energy of (*b*) has increased relatively to that of (*d*), *i.e.*, the double-helical form has become relatively less stable at the lower ionic strengths. The same conclusion has also been reached on other grounds [5, 16, 21] and has been attributed to a weakening of the structure when the repulsion between the phosphate charges is enhanced at low μ.

The quantity $(\Delta G_5^\circ - \Delta G_4^\circ)$ can also be regarded as the sum of two factors, one independent of and the other dependent on μ, so that, with the same notation as in (6):

$$(\Delta G_5^\circ - \Delta G_4^\circ) = [(G_f^\circ - G_e^\circ)_\nu - (G_d^\circ - G_b^\circ)]_\nu + [(G_f^\circ - G_e^\circ)_\mu - (G_d^\circ - G_b^\circ)_\mu] \quad . \quad (7)$$

$(\Delta G_5^\circ - \Delta G_4^\circ)$ is negative at all μ, which means that the $-NH{\cdot}CO-$ groups in the denatured molecule [equation (6)] act as stronger acids than do the same groups when in the double helix. For high μ, when the "electrostatic" terms are negligible, this implies that, in the alkaline branches of the titration curves ($h < 0$), the complementary hydrogen bonds are stabilising, relatively to the denatured form (*d*), the helical form (*b*) which is acting as an acid [equation (5)]; in the acid branches ($h > 0$), these complementary hydrogen bonds again stabilise, relatively to (*d*), the helical form (*b*) which here, in contrast, acts as the conjugate base [equation (1)]. This is equivalent to saying that $(G_d^\circ - G_b^\circ)_\nu$ is positive; if this is so, $(G_a^\circ - G_c^\circ)_\nu$ and $(G_e^\circ - G_f^\circ)_\nu$ could be positive (which implies that the charged helical form has a higher free energy than the charged denatured form), or these quantities could be negative but numerically small in comparison with $(G_d^\circ - G_b^\circ)_\nu$. Rice and Doty [19] have calculated from the viscosity changes when sodium deoxyribonucleate is heated (at $\mu \sim 0{\cdot}15$) that, if it is assumed that (*b*) $\rightleftharpoons$ (*d*) at different temperatures, $\Delta H = H_d - H_b = 110$ kcal./mole and $\Delta S = S_d - S_b = 300$ cal./degree, which makes $\Delta G = G_d^\circ - G_b^\circ = +2{\cdot}1$ kcal./mole at 25°. Such calculations, based as they are only on viscosity measurements, are very provisional numerically, but they are consistent with the above suggestion that $(G_d^\circ - G_b^\circ)$ is positive at 25°.

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The University, Birmingham, 15. [*Received, May 8th*, 1958.]

* *Erratum.* The values given in Part V [6] for this free-energy difference ($\Delta G_{III}^\circ - \Delta G_{IV}^\circ$ in the notation there) are incorrect (+200 to +480 cal./mole) and should read +1·0 to +2·5 kcal./mole.

[23] Peacocke and Lifson, *Biochim. Biophys. Acta*, 1956, **22**, 191.

831. *Catalytic Oxidation of Carbohydrates. Some Properties of Potassium α-D-Glucopyranuronate 1-(Dipotassium Phosphate).*

By S. A. Barker, E. J. Bourne, J. G. Fleetwood, and M. Stacey.

The actions of alkaline intestinal phosphatase and potato phosphorylase on potassium α-D-glucopyranuronate 1-(dipotassium phosphate) have been investigated. Acid-hydrolysis constants have been determined of both this sugar phosphate and α-D-glucopyranose 1-(dipotassium phosphate). The platinum–O_2 method of oxidation is shown to be inhibited by ammonium carbonate and glycine and to be inapplicable to certain nitrogen-containing carbohydrates.

Gaseous oxygen in the presence of platinum black suspended in a neutral or slightly alkaline solution has been widely applied to the oxidation of carbohydrates.[1-5] The use of a platinum catalyst in the synthesis of potassium α-D-glucopyranuronate 1-(dipotassium phosphate) [GA-1-P], a compound of potential interest for biosynthesis, was described independently by Barker, Bourne, and Stacey [4] and by Marsh.[5] We now wish to report some properties of this phosphate and the inhibition of platinum–oxygen oxidation by certain nitrogenous compounds.

Crystalline potassium α-D-glucopyranuronate 1-(dipotassium phosphate) dihydrate was isolated in 45% yield from α-D-glucopyranose 1-(dipotassium phosphate) and showed optimum stability at pH 8. Removal of potassium ions on an ion-exchange resin, and hydrolysis of the free acid with formic acid, readily gave α-D-glucurono-γ-lactone. Alkaline intestinal phosphatase [6] completely hydrolysed both this phosphate and α-D-glucose 1-(dipotassium phosphate) [G-1-P]. The addition of disodium hydrogen phoshate retarded hydrolysis but did not prevent its going to completion (Table 1). By hydrolysis of the uronate phosphate GA-1-P with phosphatase, glucurone was obtained in 81% yield corresponding to an overall yield of 36% from glucose 1-phosphate.

The fact that potato phosphorylase [7] synthesised amylose from the glucose phosphate G-1-P prompted us to investigate the possibility of synthesising a polyuronide by the action of phosphorylase on the uronate phosphate GA-1-P. This enzyme, to which ammonium molybdate was added to inhibit the phosphatase impurity, had however no action on the uronate phosphate but from the glucose phosphate 82% of the theoretical amount of phosphorus was liberated, and a substance which gave a blue stain with iodine was formed in the digest.

The stabilities of the two phosphates in acid solution were compared. A pH of 1·5 or 2·0 was found to give a convenient rate of hydrolysis at 61°. Log $(a - x)$ was linear with respect to t (where a = initial concentration and x = amount of substance hydrolysed at time t) in each case, showing that the reactions were of the first order. From the equation for a first-order reaction $t = \frac{1}{k}\ln a - \frac{1}{k}\ln (a - x)$ the constant k was calculated:

$$\text{G-1-P (pH 1·5)}, k = 1{\cdot}35 \times 10^{-4} \text{ sec.}^{-1}$$
$$\text{G-1-P (pH 2·0)}, k = 3{\cdot}65 \times 10^{-5} \text{ sec.}^{-1}$$
$$\text{GA-1-P (pH 1·5)}, k = 6{\cdot}03 \times 10^{-6} \text{ sec.}^{-1}$$
$$\text{GA-1-P (pH 2·0)}, k = 3{\cdot}86 \times 10^{-6} \text{ sec.}^{-1}$$

[1] Mehltretter, Rist, and Alexander, U.S.P. 2,472,168.
[2] Mehltretter, Alexander, Mellies, and Rist, *J. Amer. Chem. Soc.*, 1951, **73**, 2424.
[3] Overend, Shafizadeh, Stacey, and Vaughan, *J.*, 1954, 3633.
[4] Barker, Bourne, and Stacey, *Chem. and Ind.*, 1951, 970.
[5] Marsh, *J.*, 1952, 1578.
[6] Schmidt and Thannhauser, *J. Biol. Chem.*, 1943, **149**, 369.
[7] Barker, Bourne, Wilkinson, and Peat, *J.*, 1950, 84.

Thus the introduction of a carboxylic acid group at $C_{(6)}$ increases the stability towards acid by a factor of 10. This feature is probably related to the well-known acid stability of aldobiuronic acids.[8]

Two attempts to oxidise α-D-glucosylamine by oxygen and a platinum catalyst were unsuccessful. In one attempt, in which the pH value of the reaction mixture fell to 4·83, the α-D-glucosylamine was completely hydrolysed to glucose. This was prevented by first passing the oxygen through a wash-bottle containing dilute ammonia. Although the pH was thus maintained between 8 and 9 and only very slight hydrolysis of the glucosylamine occurred, no oxidation products could be detected. This was not due to the high pH value since it has been found [9] that the catalyst functioned efficiently over the range pH 3—10. Also in the previous experiment, in which glucose had been formed by hydrolysis of the glucosylamine, no saccharic acid could be detected by paper chromatographic analysis. D. J. C. Wood (personal communication) also failed to oxidise methyl *N*-benzyloxycarbonyl-α-D-glucosaminide and methyl *N*-acetyl-α-D-glucosaminide by the same method and it seemed probable that nitrogenous substances in some way inhibited the oxidation.

To investigate this, attempts were made to oxidise methyl α-D-glucopyranoside in the presence and absence of ammonium carbonate or glycine. No oxidation was observed in the presence of either of these substances, and when ammonium carbonate was added to partly oxidised methyl α-D-glucopyranoside there was no further change in the optical rotation of the solution (Table 4). The catalyst which had been used for the attempted oxidation in the presence of ammonium carbonate was recovered and washed with hot water, before being incorporated into a fresh solution of methyl α-D-glucopyranoside. Initially (first 1·5 hr.) little reaction occurred but after 6 hr. the Tollens test [10] became positive and there was a definite decrease in optical rotation and pH. These results indicated that nitrogenous compounds were in some way adsorbed on to the catalyst and rendered it inactive, and that the adsorbed substance was only removed slowly. This method of oxidation therefore seems to be inapplicable to nitrogen-containing carbohydrates.

Finally to confirm that this method results in oxidation of primary, and not secondary, alcohol groups dulcitol was oxidised to mucic acid (yield 57·8%) which was further characterised by conversion into dimethyl 2 : 3-4 : 5-di-*O*-methylenemucate.

Experimental

Potassium α-D-Glucopyranuronate 1-(Dipotassium Phosphate).—α-D-Glucose 1-(dipotassium phosphate) dihydrate (5·0 g.) was oxidised with a stream of purified oxygen in the presence of a platinum–charcoal catalyst [9] (1·6 g.) suspended in water (200 c.c.) at 61° for 92 hr. After removal of the catalyst, the solution (pH 5·60) was made slightly alkaline with potassium hydroxide and concentrated to *ca.* 30 c.c., and a syrup was precipitated by addition of methanol (150 c.c.). After purification by eight reprecipitations from aqueous methanol, potassium α-D-glucopyranuronate 1-(dipotassium phosphate) dihydrate (2·6 g.) crystallised in rosettes of fine needles, $[\alpha]_D^{19}$ +53·6° (*c* 1·54 in water) (Found: C, 16·5; H, 3·0; P, 7·3; K, 27·9. Calc. for $C_6H_{12}O_{12}PK_3$: C, 17·0; H, 2·8; P, 7·3; K, 27·6%).

Conversion into Glucurone by Acid-hydrolysis.—Potassium α-D-glucopyranuronate 1-(dipotassium phosphate) dihydrate (0·55 g.) in water (5 c.c.) was passed through a column of ion-exchange resin (Zeo-Karb 215) to give α-D-glucopyranuronic acid 1-(dihydrogen phosphate) which, after concentration to a syrup (0·37 g.), was hydrolysed with 90% formic acid for 4 hr. at 100°. Removal of formic acid by distillation *in vacuo*, decolorisation with charcoal, and crystallisation from methanol of the syrup obtained after concentration gave α-D-glucurono-γ-lactone (0·21 g.), m. p. and mixed m. p. 170—172°.

[8] O'Dwyer, *Biochem. J.*, 1934, **28**, 2116.
[9] Merck and Co., U.S.P. 2,483,251.
[10] Tollens, *Ber.*, 1908, **41**, 1788.

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Conversion into Glucurone by Alkaline Phosphatase.—A digest was prepared containing potassium α-D-glucopyranuronate 1-(dipotassium phosphate) dihydrate (0·5 g.), 0·2M-borate buffer (pH 9·24; 10 c.c.), and a solution (10 c.c.) of alkaline phosphatase (20 mg.) in a total volume of 30 c.c. The alkaline phosphatase had been extracted from the intestines of ten calves by Schmidt and Thannhäuser's method [6] and liberated 217 μg. of *p*-nitrophenol per minute per mg. of nitrogen in the preparation under the standard conditions described by Axelrod.[11] The digest was incubated at 37°, and the progress of the hydrolysis followed by the removal, at intervals, of aliquot portions for the determination of inorganic phosphate.[12] After 4 hr., when the degree of hydrolysis was 99·3%, enzyme action was arrested by heating the solution at 100° for 5 min. Most of the liberated phosphate was removed by precipitation with magnesia mixture, and the filtrate concentrated *in vacuo* to a syrup which was extracted with methanol. After evaporation the methanol extract gave crystalline α-D-glucurono-γ-lactone (0·18 g.), m. p. and mixed m. p. 170—171°.

Effect of Phosphate on the Enzymic Hydrolysis of the Two Phosphates by Alkaline Phosphatase.—Three digests, containing 0·01M-α-D-glucopyranuronate 1-phosphate (2 c.c.), 0·2M-borate buffer (pH 9·26, 2 c.c.), and a solution (2 c.c.) of alkaline phosphatase (0·2 mg.) were prepared. In the second and third of these digests (total volume, 8 c.c.), 0·00603M-disodium hydrogen phosphate (1 c.c. and 2 c.c. respectively) was incorporated. Three similar digests, in which the uronate phosphate was replaced by α-D-glucose 1-phosphate, were also prepared and all were incubated at 37°. Aliquot portions were removed at intervals for the determination of the degree of hydrolysis. The results are given in Table 1.

TABLE 1. *Enzymic hydrolysis of α-D-glucose 1-phosphate* (G-1-P) *and α-D-glucopyruronate 1-phosphate* (GA-1-P) *in the presence of phosphate.*

Time (hr.)	No added phosphate	Phosphate 1 c.c.	Phosphate 2 c.c.
	Hydrolysis (%) *of* GA-1-P		
1·5	99·8	99·5	96·4
3·0	100·2	101·0	98·5
6·0	99·8	101·0	99·3
24·0	101·0	100·5	100·3
	Hydrolysis (%) *of* G-1-P		
1·5	93·5	89·8	84·2
5·0	101·0	101·0	98·4
22·0	100·2	101·0	100·2

TABLE 2. *Action of phosphorylase.*

	G-1-P		GA-1-P
Time (hr.)	A.V. (680 mμ)	Inorg. P liberated (%)	Inorg. P liberated (%)
1	0·013	5·3	—
20	0·168	78·7	—
92	0·292	82·0	0·5

TABLE 3. *Rates of hydrolysis by acid.*

	Hydrol. (%) of G-1-P at		Hydrol. (%) of GA-1-P at	
Time (hr.)	pH 1·50	pH 2·00	pH 1·50	pH 2·00
0·5	20·4	7·3	—	—
1·0	36·4	12·2	1·3	1·3
1·5	49·5	17·9	2·4	2·2
2·5	70·2	31·1	4·5	2·7
5·0	91·4	47·7	9·6	6·9
22·0	100·2	97·3	38·4	26·0
29·0	—	99·8	46·7	33·6
pH after 24 hr.	1·60	2·05	1·53	2·04

These phosphates were also hydrolysed with phosphatase in the presence of an approximately equimolecular concentration of glucose (for G-1-P) and glucurone (for GA-1-P). In both cases the substrate was hydrolysed completely at almost the same rate as in the absence of added glucose or glucurone.

[11] Axelrod, *J. Biol. Chem.*, 1947, **167**, 57.
[12] Allen, *Biochem. J.*, 1940, **34**, 858.

Action of Phosphorylase on the Two Phosphates.—A digest, containing potato phosphorylase solution (1 c.c.), 0·5M-citrate buffer (pH 6·0; 0·5 c.c.), 0·1M-α-D-glucose 1-phosphate (1 c.c.), 8% ammonium molybate solution (1 c.c.) and water (0·5 c.c.) was prepared. A similar digest containing α-D-glucopyruronate 1-phosphate in the place of the glucose derivative, and control digests, containing no phosphorylase, were also prepared. The four digests were incubated at 37°, and aliquot portions removed at intervals, for the determination of inorganic phosphate [12] and the iodine staining power, after inactivation of the phosphorylase with trichloroacetic acid. In the case of the control digests an equivalent amount of phosphorylase solution was added after the addition of trichloroacetic acid. The results are shown in Table 2.

Relative Stability of the Two Phosphates to Acid-hydrolysis.—Two solutions of α-D-glucose 1-(dipotassium phosphate) (20 mg.) were adjusted with hydrochloric acid to pH 1·50 and pH 2·00 respectively, in final volumes of 20 c.c. Similar solutions containing potassium α-D-glucopyranuronate 1-(dipotassium phosphate) were also prepared and all four, in glass-stoppered tubes, placed in a thermostatically controlled water-bath held at 61°. The degree of hydrolysis, measured at intervals by the withdrawal of aliquot portions for inorganic phosphate determination, is shown in Table 3.

Attempted Oxidation of α-D-Glucopyranosylamine.—α-D-Glucopyranosylamine (3 g.) was dissolved in water (200 c.c.), sodium hydrogen carbonate (1·2 mol.), and platinum–charcoal (1·0 g.) were added, and a stream of purified oxygen was passed through the suspension at 61°. During the reaction the pH fell from 8·61 to 4·83, and paper chromatography of the products showed that the α-D-glucopyranosylamine had been hydrolysed completely to glucose. No sugar, other than glucose, could be detected and the solution gave a negative Tollens test [10] for uronic acid.

The experimental procedure was modified by passing the oxygen through a dilute solution of ammonia before its injection into the reaction mixture. The pH value then increased from 8·10 to 9·04 during the reaction, and remained at this value. After 90 hr. paper chromatography showed slight hydrolysis of α-D-glucopyranosylamine to di-α-D-glucopyranosylamine but no other sugars could be detected, and the solution gave a negative test for uronic acids.

Oxidation of Methyl α-D-Glucopyranoside in the Presence of Nitrogenous Compounds.—Four solutions, each containing methyl α-D-glucopyranoside (0·49 g.) and sodium hydrogen carbonate (0·25 g.) in water (50 c.c.), were prepared, and freshly prepared catalyst (0·35 g.) was added to three of these (A, B, and C). Ammonium carbonate (0·14 g.) was incorporated into two of these solutions as follows: (A) control, no ammonium carbonate added, (B) ammonium carbonate

TABLE 4. *Oxidation of methyl α-D-glucopyranoside in the presence of ammonium carbonate.*

Time	A		B		C		D	
(hr.)	pH	$[\alpha]_D^{17}$	pH	$[\alpha]_D^{17}$	pH	$[\alpha]_D^{17}$	pH	$[\alpha]_D^{17}$
0	8·66	+157°	8·97	+157°	8·66	+157°	8·63	+159°
0·25	7·14	122	9·33	157	7·04	118	9·02	151
0·75	6·31	104	9·52	157	6·13 *	100	9·14 †	151
1·0	—	—	—	—	8·89	90	—	—
1·5	5·57	86	9·68	151	9·08	88	9·16 †	149
3·0	5·25	75	9·74	147	9·21	90	—	—
5·0	5·08 *	73	9·75 †	151	9·24	90	—	—
6·0	—	—	—	—	—	—	8·13 *	112

* Uronic acid test positive. † Uronic acid test negative.

added at commencement of oxidation, (C) ammonium carbonate added after 1 hr. The three solutions A, B, and C were oxidised as previously described and the progress of the reaction in each case was followed by changes in pH value and optical rotation (Table 4). The catalyst from solution B was recovered, washed, and dried, and added to the fourth solution (D) which was then oxidised in the usual way.

When the experiment was repeated with glycine in place of ammonium carbonate, similar results were obtained.

Oxidation of Dulcitol.—Dulcitol (2·7 g.) was dissolved in a solution of sodium hydrogen carbonate (1·5 g.) in water (100 c.c.), and oxidised in a stream of oxygen at a platinum–charcoal catalyst [9] (1·4 g.). During the reaction the pH fell from 8·46 to 5·00; at this point a further amount (1·3 g.) of sodium hydrogen carbonate was added, the pH of the solution increasing to

7·6. The reaction was continued until a constant pH (6·4) was reached after 15 hr. The suspension was made alkaline to phenolphthalein with sodium hydroxide, and the catalyst was removed and washed with hot distilled water. The filtrate and washings were concentrated *in vacuo* and made acid with hydrochloric acid and, the precipitated solid was removed. After purification, mucic acid (1·8 g., 57·8%), m. p. and mixed m. p. 213°, was isolated. This was further characterised by conversion into dimethyl 2 : 3-4 : 5-di-*O*-methylenemucate, m. p. and mixed m. p. 101°.

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832. *Tetronic Acids and Related Compounds. Part IV.* Friedel–Crafts Reaction and Fries Rearrangement.*

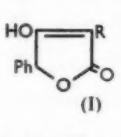
By L. J. HAYNES and J. W. M. JAMIESON.

γ-Substituted tetronic acids undergo *C*-acylation with acetyl chloride in presence of Friedel–Crafts catalysts, and their enol acetates and benzoates are rearranged to α-acyl derivatives. These reactions are of value for the preparation of γγ-disubstituted α-acyltetronic acids.

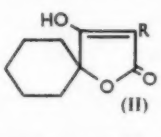
APPLICATIONS of the Friedel–Crafts reaction and the Fries rearrangement to tetronic acids have not previously been reported, but in view of the known susceptibility of tetronic acid to electrophilic substitution [1] it seemed that they might offer useful additions to existing methods [2,3] for the synthesis of α-acyltetronic acids.

The condensation of γ-phenyltetronic acid (I; R = H) with acetyl chloride in presence of aluminium, stannic, or zinc chloride was investigated under various conditions. The crude acid product was examined by paper chromatography, best with butan-1-ol–ammonia–pyridine–saturated aqueous sodium chloride;[4] tetronic acid derivatives were detected photographically by virtue of their ultraviolet absorption; this technique afforded rapid and convenient determination of the optimum conditions for acylation.

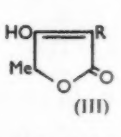
Acylation occurred with any of the three catalysts, the optimum conditions being to reflux γ-phenyltetronic acid with stannic chloride (1·3 mols.) in an excess of acetyl chloride for 4 hours. The α-acetyl-γ-phenyltetronic acid (I; R = Ac) isolated was



(I)



(II)



(III)

identified by comparison with samples prepared from acetylmandelyl chloride and ethyl sodioacetoacetate or ethyl β-aminocrotonate (by Rebstock and Sell's modification [3] of Benary's method [2]). The separation of product from starting material required several

* Part III, *J.*, 1956, 4556.

[1] Wolff and Schwabe, *Annalen*, 1896, **291**, 226; Wolff and Lüttringhaus, *ibid.*, 1900, **312**, 119.

[2] Benary, *Ber.*, 1909, **42**, 3912; Baker, Grice, and Jensen, *J.*, 1943, 241; Lecoq, *Compt. rend.*, 1946, **222**, 183; Reuter and Welch, *J. Proc. Roy. Soc. N.S.W.*, 1939, **72**, 120; Lacey, *J.*, 1954, 832; Haynes, Plimmer, and Stanners, *J.*, 1956, 4661.

[3] Rebstock and Sell, *J. Amer. Chem. Soc.*, 1952, **74**, 274.

[4] Bray, Lake, Thorpe, and White, *Biochem. J.*, 1950, **47**, 13.

recrystallisations, so the yield was poor, but better results were obtained with γγ-disubstituted tetronic acids: γγ-dimethyl- and γγ-diphenyl-tetronic acid gave (in about 50% yield) crude products which paper chromatography proved to be virtually pure α-acetyl derivatives. Surprisingly, *cyclo*hexane*spiro*-γ-tetronic acid (II; R = H) appeared not to undergo acylation. On acylation of γ-methyltetronic acid (III; R = H) there were indications of the formation of the α-acetyl derivative (III; R = Ac) but it could not be isolated. Nevertheless we treated γ-methyltetronic acid with 2-methoxycarbonylpropionyl chloride in the hope of obtaining carolinic acid (III; R = CO·[CH_2]$_3$·CO_2H): though paper chromatography showed the presence of a compound with the same R_F as carolinic acid yet this product could not be isolated.

Attempted alkylation of γ-phenyltetronic acid with ethyl bromide and stannic chloride or with benzyl chloride and aluminium chloride was unsuccessful, the acid being recovered.

Fries rearrangement of (enol) acetates and benzoates of a number of tetronic acids was also found to occur: again stannic chloride was a better catalyst than zinc or aluminium chloride, and better results were obtained with the γγ-disubstituted tetronic acids. The acetates of γγ-diphenyl- and γγ-dimethyl-tetronic acid gave a 63% and a 71% yield of the respective α-acetyl derivatives, identical with those obtained by Friedel–Crafts condensation. The benzoates of γγ-dimethyltetronic and *cyclo*hexane*spiro*-γ-tetronic acid gave the α-benzoyl derivatives in 77% and 71% yield respectively. Chromatography of the crude products from the rearrangement of the enol benzoates of γ-phenyl- and γγ-diphenyl-tetronic acids showed that a new substance had been formed in each case: the products however contained much benzoic and tetronic acids and the α-benzoyl compounds were not obtained pure.

Experimental

Light petroleum used had b. p. 60—80° unless otherwise stated.

α-Acetyl-γ-phenyltetronic Acid (I; R = Ac).—(*a*) Ethyl acetoacetate (13·0 g.) was added dropwise with stirring to sodium (2·3 g.) in dry ether (100 ml.) and the mixture set aside overnight. Acetylmandelyl chloride [5] (21·2 g.) in dry ether (50 ml.) was added dropwise with stirring and cooling in ice. The mixture was stirred for 3 hr. at room temperature, then shaken with ice (100 g.). The aqueous layer was separated and extracted twice with ether, and the combined ethereal extracts were washed with water, aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). Removal of the ether left a yellow oil (40 g.). This product (6 g.) was treated in ethanol with aqueous 0·5N-sodium hydroxide (2 mols.) and set aside for 24 hr. at room temperature, then acidified with dilute sulphuric acid. α-Acetyl-γ-phenyltetronic acid was precipitated. After recrystallisation from light petroleum it (0·84 g., 26% based on acetylmandelyl chloride) had m. p. 102—104° (Lecoq [2] gives m. p. 104°).

(*b*) Ethyl β-aminocrotonate [6] (48·0 g.) in dry ether (175 ml.) and dry pyridine (32·8 g.) at −50° to −60° was treated with acetylmandelyl chloride [5] (88·3 g.) in dry ether (80 ml.) during 2 hr., then stirred overnight while it was allowed to come to room temperature. A colourless solid separated. The mixture was shaken with chloroform (80 ml.) and water (200 ml.), and the organic layer separated and dried (Na_2SO_4). Removal of the solvents gave a gum (72·0 g.) which crystallised on trituration with dry ether. Recrystallised from ether–light petroleum it had m. p. 86—89°. It (5·0 g.) was set aside with 10% aqueous sodium hydroxide at room temperature for 24 hr. Acidification with dilute hydrochloric acid and extraction gave α-acetyl-γ-phenyltetronic acid (2·4 g., 48%), m. p. 102—104° (from light petroleum). Hydrolysis with hot alkali or with acid at room temperature gave poorer yields. The acetyl compound gave a yellow precipitate with ferric chloride and a deep-red colour with sodium nitroprusside. It

[5] Thayer, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 12.
[6] Mentzer, Billet, Molho, and Xuong, *Bull. Soc. chim. France*, 1945, **12**, 161; Tinker and Whatmough, *J. Amer. Chem. Soc.*, 1952, **74**, 5235.

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formed an *oxime*, m. p. 162—164° [from ethyl acetate–light petroleum (b. p. 100—120°)] (Found: N, 5·8. $C_{13}H_{11}O_4N$ requires N, 6·0%).

cyclo*Hexane*spiro-*γ-tetronic Acid* (II; R = H) (with Dr. A. H. Stanners).—A mixture of ethyl 1-hydroxy*cyclo*hexanecarboxylate [7] (34·4 g.), acetic anhydride (30 g.), and concentrated sulphuric acid (3 drops) was set aside for 5 hr., then refluxed for 15 min. Ether was added, and the solution washed with aqueous sodium hydrogen carbonate, then with water, and dried (Na_2SO_4). Distillation gave *ethyl* 1-*acetoxy*cyclo*hexanecarboxylate* (33·6 g., 77%), b. p. 117—121°/10 mm., n_D^{20} 1·4484 (Found: C, 62·1; H, 8·6. $C_{11}H_{18}O_4$ requires C, 61·7; H, 8·5%).

This ester (16·1 g.) in dry ether (25 ml.) was added during 30 min. to an ethereal suspension of di*iso*propylaminomagnesium bromide [8] (from magnesium 2·43 g., ethyl bromide 10·9 g. and di*iso*propylamine 10·1 g.); a light green sticky mass separated. The mixture was refluxed for another 1 hr. and set aside overnight. Ice-cold 3N-hydrochloric acid (100 ml.) was added, and the aqueous layer separated, saturated with sodium chloride, and extracted with ether. The combined ether solutions were extracted with aqueous sodium hydrogen carbonate, and the alkaline extract acidified, to give a *cyclo*hexane*spiro*-γ-tetronic acid. Extraction with ethyl acetate gave a total yield of 5·6 g. (45%), prisms (from aqueous ethanol), m. p. 195—196° (Jones and Whiting [9] give m. p. 198°). It gave a light purple colour with aqueous sodium nitrite.

Friedel–Crafts Reactions.—In acetylations, the most effective procedure was to mix the tetronic acid with some excess of acetyl chloride, to add stannic chloride (1·3 mol.), and to heat the red solution under reflux for 3—4 hr. The mixture was poured into ice-cold 5N-hydrochloric acid and set aside until it came to room temperature, then filtered and extracted with chloroform, and the extract shaken with concentrated aqueous sodium hydrogen carbonate. (At this stage, much inorganic material was removed with difficulty by filtration.) Acidification of the carbonate layer with concentrated hydrochloric acid produced a white opacity. The mixture was extracted with chloroform, and the extract dried (Na_2SO_4) and evaporated at reduced pressure. The extent of acylation was then estimated by paper chromatography of this crude residue, with butan-1-ol–ammonia (*d* 0·880)–pyridine–saturated aqueous sodium chloride (40 : 30 : 80 : 50 v/v).[4] Spots were located by making contact prints of the chromatograms by exposure (3—4 sec.) to ultraviolet light.

In this way γ-phenyltetronic acid (13·2 g.) gave a crude semicrystalline product which after five recrystallisations from light petroleum gave chromatographically pure α-acetyl-γ-phenyltetronic acid (3·2 g., 20%), m. p. 101—104° (mixed m. p. 100—102°) (Found: C, 66·5; H, 4·7. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6%).

γγ-Diphenyltetronic acid (2·0 g.) gave virtually pure α-acetyl-γγ-diphenyltetronic acid (1·3 g., 56%) which, crystallised readily from light petroleum (b. p. 60—80°), had m. p. 99—101° (Lacey [2] gives m. p. 102°).

γγ-Dimethyltetronic acid (2·6 g.) gave a crystalline crude product (2·0 g., 58%) which, recrystallised from light petroleum (b. p. 80—100°), gave pure α-acetyl-γγ-dimethyltetronic acid, m. p. 64° (Lacey [2] gives m. p. 64—65°).

Attempts at benzoylation, using benzoyl chloride and stannic chloride, were unsuccessful owing partly to the amount of benzoic acid produced in the working up; some conversion was, however, detectable chromatographically.

Preparation of Enol Esters.—Enol acetates were prepared by mixing the tetronic acid with a small excess of acetic anhydride and adding a few drops of concentrated sulphuric acid. The solution was kept at room temperature for a few hours, then diluted with chloroform. The solution was washed with saturated sodium hydrogen carbonate solution, from which a little unchanged tetronic acid was recovered by acidification. The chloroform solution was dried (Na_2SO_4) and solvent removed at reduced pressure. The residue then crystallised from light petroleum.

In this way were prepared: 3-*acetoxy*-2 : 5-*dihydro*-5-*oxo*-2 : 2-*diphenylfuran* (68%), m. p. 105° (Found: C, 73·6; H, 4·7. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·8%); 3-*acetoxy*-2 : 5-*dihydro*-2 : 2-*dimethyl*-5-*oxofuran* (79%), m. p. 59—60° (Found: C, 56·7; H, 6·2. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%); and cyclo*hexane*spiro-2-(2 : 5-*dihydro*-5-*oxofuran*) (74%), m. p. 93° (Found: C, 63·1; H, 6·8. $C_{11}H_{14}O_4$ requires C, 62·9; H, 6·7%).

[7] Billimoria and Maclagan, *J.*, 1951, 3069.
[8] Haynes and Stanners, *J.*, 1956, 4103.
[9] Jones and Whiting, *J.*, 1949, 1421.

Enol benzoates were prepared by the Schotten–Baumann method. The tetronic acid in sodium carbonate solution was shaken for 5—10 min. with 1 mol. of benzoyl chloride and kept for 2—3 days at room temperature. The brown resin which resulted was washed by suspension in sodium carbonate solution, then recovered and dried. Crystallisation from light petroleum gave the pure enol benzoate.

In this way were prepared: 3-*benzoyloxy*-2 : 5-*dihydro*-5-*oxo*-2-*phenylfuran* (69%), m. p. 93° (Found: C, 73·2; H, 4·6. $C_{17}H_{12}O_4$ requires C, 72·8; H, 4·3%), and -2 : 2-*diphenylfuran* (76%), m. p. 165° (Found: C, 77·6; H, 4·8. $C_{23}H_{16}O_4$ requires C, 77·5; H, 4·5%); 3-*benzoyloxy*-2 : 5-*dihydro*-2-*methyl*- (62%), m. p. 39—43° (Found: C, 65·9; H, 4·5. $C_{12}H_{10}O_4$ requires C, 66·0; H, 4·6%), and -2 : 2-*dimethyl*-5-*oxofuran* (73%), m. p. 130—131° (Found: C, 66·9; H, 5·0. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%); and cyclo*hexane*spiro-2-(3-*benzoyloxy*-2 : 5-*dihydro*-5-*oxofuran*) (82%), m. p. 125—128° (Found: C, 71·0; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·5; H, 5·9%).

Fries Rearrangements.—For acetates the best method was to suspend the ester (0·01 mol.) in dry nitrobenzene, add the catalyst (0·013 mol.), and heat the whole at 100° for 2—3 hr. After working up as for the Friedel–Crafts reactions, the extent of conversion was estimated chromatographically.

With zinc chloride as catalyst, γ-phenyltetronic acid acetate (Haynes *et al.*[2]) gave crude α-acetyl-γ-phenyltetronic acid containing about 10% of γ-phenyltetronic acid, inseparable by crystallisation. Ten chromatograms on 3MM. Whatman No. 1 paper, the pure acetyl compound being recovered by spraying the papers with dilute hydrochloric acid and eluting the appropriate areas with ethanol, gave the α-acetyl compound, m. p. and mixed m. p. 104—105° (from light petroleum).

With stannic chloride as catalyst, γγ-diphenyltetronic acid acetate gave α-acetyl-γγ-diphenyltetronic acid (63%) which after one crystallisation from light petroleum (b. p. 80—100°) was chromatographically pure and had m. p. and mixed m. p. 64° (Found: C, 56·9; H, 6·1. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). The *spiro*-acid acetate did not rearrange. γ-Methyltetronic acid acetate gave a mixture of about equal parts of α-acetyl-γ-methyl- and γ-methyltetronic acid, which with phenylhydrazine in boiling benzene gave yellow α-acetyl-γ-methyltetronic acid phenylhydrazone, m. p. 163—165° (Lacey [2] gives m. p. 165°).

For rearrangements of the benzoates, similar conditions were used, save that heating was usually for 4 hr. γγ-Dimethyltetronic acid benzoate gave 4-*benzoyl*-2 : 5-*dihydro*-2 : 2-*dimethylfuran* (77%), m. p. 77°, chromatographically pure after recrystallisation from light petroleum (b. p. 80—100°) (Found: C, 67·2; H, 5·2. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). The *spiro*-acid benzoate similarly gave cyclo*hexane*spiro-2-(4-*benzoyl*-2 : 5-*dihydro*-5-*oxofuran*) (71%), m. p. 119° [from ethyl acetate–light petroleum (b. p. 80—100°)] (Found: C, 70·8; H, 6·3. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

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XUM

833. *The Crystal Structure of the Mercury Dithizone Complex.*

By MARJORIE M. HARDING (*née* AITKEN).

The mercury derivative of dithizone crystallises from aqueous pyridine as deep red solvated needles, $Hg(C_{13}H_{11}N_4S)_2,2C_5H_5N$. These have been studied by *X*-ray diffraction. They are orthorhombic, with $a = 35{\cdot}30$, $b = 36{\cdot}30$, $c = 5{\cdot}40$ Å, and space group *Fdd*2. The main features of the structure have been determined from Fourier projections down the *c*-axis and from a limited three-dimensional Fourier series. In the molecule of mercury dithizone, the mercury is bonded to one sulphur atom of each dithizone group; the Hg–S bond lengths are both 2·41 Å, and the S–Hg–S bond angle is 155°. A nitrogen atom from each azo-group is weakly co-ordinated to the mercury atom, making, with the sulphur atoms, a rather distorted tetrahedron around it. The dithizone groups are in an extended arrangement with no intramolecular hydrogen bonding.

ALTHOUGH dithizone, NHPh·NH·CS·N:NPh, is a common reagent for the colorimetry of certain metals, the structure of the metal derivatives has remained uncertain. A crystal-structure determination by *X*-ray methods was therefore undertaken, and the mercury derivative, $Hg(C_{13}H_{11}N_4S)_2$, was chosen because it could be obtained suitably crystalline. The deep red crystals contain pyridine of crystallisation which, as seen from their deterioration, they slowly lose on standing in air. They are orthorhombic, with cell dimensions $a = 35{\cdot}30 \pm 0{\cdot}03$, $b = 36{\cdot}30 \pm 0{\cdot}03$, $c = 5{\cdot}40 \pm 0{\cdot}02$ Å. The needle axis is parallel to *c*; the space group is *Fdd*2. A density, 1·58 g. cm.$^{-3}$, was found by flotation in aqueous potassium iodide solution, a procedure in which the loss of a little pyridine would be expected. The calculated density for eight molecules $Hg(C_{13}H_{11}N_4S)_2$ and sixteen molecules of pyridine per unit cell is 1·66 g. cm.$^{-3}$; for eight unsolvated molecules it would be 1·35 g. cm.$^{-3}$. The mercury atoms must lie in special positions on the two-fold axis. Further, the *z* parameter can be chosen arbitrarily as zero. The other atoms are in general positions, and the two dithizone residues of one molecule are related by a two-fold axis.

The *X*-ray photographs show a remarkably even fall in intensity of the *X*-ray reflections with increasing angle of reflection, because the scattering is predominantly by the mercury atoms at special positions in the lattice. Relatively small variations in this even fall are due to the contributions of the rest of the molecule; consequently the accuracy with which the co-ordinates of the light atoms could be found was limited.

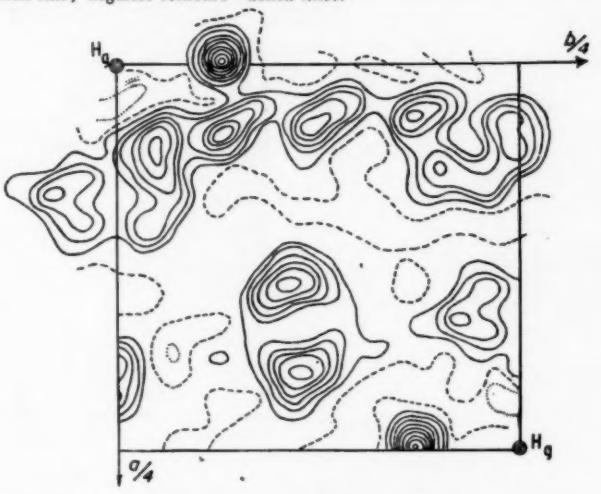
The intensities of the reflections in the layers with $l = 0$, 1, 2, and 3 were measured by visual estimation and converted to $|F(hkl)|$ values.

STRUCTURE DETERMINATION

(I) *The Electron-density Projection down the* 001 *Axis.*—A Patterson projection down the *c* axis confirmed the mercury positions. An electron-density projection was then calculated, using those terms whose signs are determined by the mercury atoms; it showed the sulphur atom clearly and one benzene ring. Some, and eventually all, of the remaining terms were then added, and the projection was further improved by " subtracting " the mercury atom to eliminate their diffraction effects. Thus the position of the remainder of the dithizone group was found, and also that of a molecule of pyridine of crystallisation. The final projection is shown in Fig. 1, and the atomic arrangement in Fig. 4. Table 1 gives the observed and calculated structure factors, $F(hk0)$. The agreement factor, *R* for all reflections (158) decreased from 27% for the mercury atom positions alone, to 12% in the present structure; the *R* factor for the 23 reflections to which mercury does not contribute, fell from over 50% in the first partial structure to 29% in the present structure.

(II) *Distribution of Atoms in Three Dimensions.*—The projection shows the extended arrangement of the dithizone group, the sulphur atom bonded to mercury, and a nitrogen atom fairly close to mercury. It cannot show whether the group S–Hg–S is linear; to do

FIG. 1. *Electron-density projection.* $\rho(xy)$, *down the* c*-axis with the mercury atom at* (0,0) *subtracted. Contours at intervals of* 1 e Å^{-2} *starting at* 2 e Å^{-2} (*and at* 2 e Å^{-2} *intervals on the sulphur atom*); *zero contour—broken line; negative contours—dotted lines.*



this the atomic arrangement in the third dimension must be found. Here, calculation of the electron density in three dimensions was necessary, since projections down the *a* and *b* axes of the unit cell, both about 35 Å long, could not show resolved atomic positions.

In three dimensions the structure is asymmetric, and the use of phase angles calculated

TABLE 1. *Observed and calculated structure factors* (*one quarter of absolute values*).

h	k	l	F (obs.)	F (calc.)
4	0	0	182	219
8	0	0	50	54
12	0	0	92	84
16	0	0	113	104
20	0	0	125	130
24	0	0	104	95
28	0	0	97	121
32	0	0	54	68
2	2	0	180	202
6	2	0	111	118
10	2	0	202	206
14	2	0	151	152
18	2	0	129	136
22	2	0	121	119
26	2	0	89	88
30	2	0	63	64
34	2	0	42	47
0	4	0	161	184
4	4	0	120	112
8	4	0	102	60
12	4	0	177	178
16	4	0	139	130
20	4	0	99	94
24	4	0	58	89
28	4	0	71	66
32	4	0	60	41
2	6	0	123	119
6	6	0	58	40
10	6	0	137	144
14	6	0	78	88
18	6	0	101	103
22	6	0	71	50
26	6	0	62	47
30	6	0	54	61
34	6	0	36	34
0	8	0	182	247
4	8	0	72	79
8	8	0	74	59
12	8	0	60	22
16	8	0	93	74
20	8	0	81	102
24	8	0	57	54
28	8	0	65	49
32	8	0	37	27
2	10	0	70	81
6	10	0	135	144
10	10	0	108	99
14	10	0	110	99
18	10	0	80	65
22	10	0	55	48
26	10	0	51	48
30	10	0	60	59
0	12	0	93	60
4	12	0	147	147
8	12	0	141	143
12	12	0	121	98
16	12	0	114	103
20	12	0	90	105
24	12	0	62	74
28	12	0	63	65
32	12	0	59	57
2	14	0	139	137
6	14	0	183	174
10	14	0	158	156
14	14	0	108	110
18	14	0	117	125
22	14	0	79	80
26	14	0	64	77
30	14	0	47	73
0	16	0	164	161
4	16	0	185	201
8	16	0	125	151
12	16	0	89	61
16	16	0	124	96
20	16	0	107	105
24	16	0	82	92
28	16	0	52	68
32	16	0	48	60
2	18	0	63	60
6	18	0	119	149
10	18	0	124	122
14	18	0	124	125
18	18	0	82	87
22	18	0	86	90
26	18	0	67	62
30	18	0	36	44
4	20	0	68	43
8	20	0	92	101
12	20	0	82	83
16	20	0	75	83
20	20	0	57	61
24	20	0	42	58
28	20	0	37	43
2	22	0	41	28
6	22	0	81	90
10	22	0	67	78
14	22	0	48	55
18	22	0	35	25
22	22	0	58	41
26	22	0	42	54
0	24	0	53	49
4	24	0	62	76
8	24	0	59	66
12	24	0	58	47
16	24	0	42	33
20	24	0	42	31
24	24	0	37	38
0	26	0	71	68
6	26	0	57	63
10	26	0	59	55
14	26	0	65	68
18	26	0	37	29
22	26	0	54	49
0	28	0	74	60
4	28	0	85	80
8	28	0	76	66
12	28	0	59	59
16	28	0	54	62
20	28	0	54	56
2	30	0	77	72
6	30	0	73	76
10	30	0	74	86
14	30	0	70	81
18	30	0	54	50
22	30	0	55	51
0	32	0	66	90
4	32	0	63	78
8	32	0	55	60
12	32	0	52	62
16	32	0	59	57
20	32	0	51	64
2	34	0	64	71
6	34	0	52	57
10	34	0	36	38
4	2	0	—	−23
8	2	0	103	−102
12	2	0	—	−6
16	2	0	—	−22
20	2	0	42	48
24	2	0	35	26
2	4	0	20	−15
6	4	0	—	4
10	4	0	24	−17
14	4	0	58	37
18	4	0	55	39
22	4	0	30	−7
4	6	0	115	−111
8	6	0	—	6
12	6	0	38	18
16	6	0	43	42
20	6	0	—	−12
24	6	0	—	8
2	8	0	65	74
6	8	0	—	21
10	8	0	—	6
14	8	0	—	16
18	8	0	—	3
22	8	0	—	−16
4	10	0	19	−5
8	10	0	—	−9
12	10	0	27	5
16	10	0	34	−33
20	10	0	—	5
2	12	0	53	−51
6	12	0	17	−18
10	12	0	19	−30
14	12	0	—	10
18	12	0	—	1
4	14	0	—	9
8	14	0	—	28
12	14	0	—	11
16	14	0	—	9
2	16	0	—	7
6	16	0	—	−25
10	16	0	—	7
14	16	0	—	0
4	18	0	41	−46
8	18	0	—	−29
12	18	0	—	−3
16	18	0	41	17
20	18	0	34	27
2	20	0	—	−12
6	20	0	—	12
10	20	0	—	−2
14	20	0	45	18
18	20	0	34	4

5 x

on the mercury-atom positions alone introduces false symmetry into the electron-density distributions. The extended distribution was calculated only after generalised projections and the section ρ(0*yz*) had been explored.

FIG. 2. *Electron density in the section* ρ(0yz) *through the sulphur atom. Contours at intervals of* 10 e Å^{-3} *on the mercury atom and* 2 e Å^{-3} *elsewhere; zero contour—broken line; negative contours—dotted lines*: (a) *using phases for mercury only—or for mercury, and sulphur at* z = 0; (b) *using phases for mercury, and for sulphur at* z = 0·10; (c) *using phases for mercury, and for sulphur at* z = 0·31.

FIG. 2*a*.

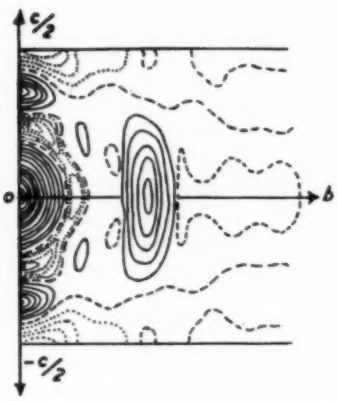


FIG. 2*c*.

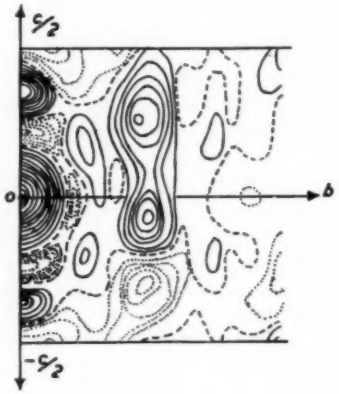
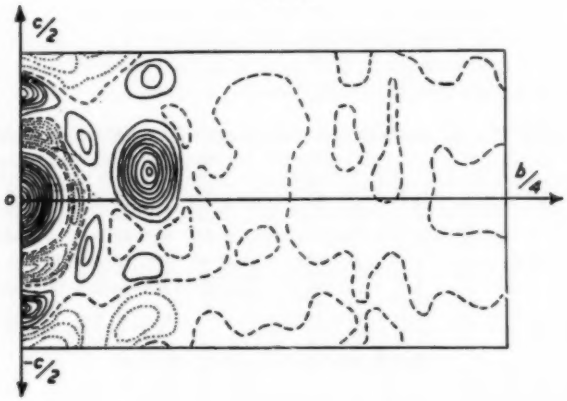


FIG. 2*b*.



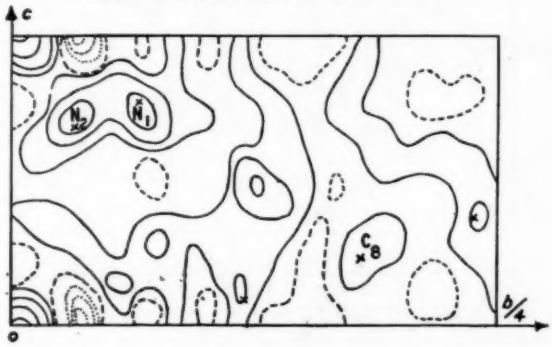
(*a*) *Generalised projections.* Since the *c* axis is short, 5·4 Å, it seemed likely that the *z* parameters of the atoms could be determined from two generalised projections calculated with the (*hk*1) and (*hk*2) F values and mercury-atom phases. In both these projections peaks occur at the expected sulphur-atom sites, but the rest of the pattern is very confused. The heights of the sulphur-atom peaks suggested that the sulphur atom is not at $z = 0$ but has a *z* co-ordinate 0·10—0·15.

(*b*) *Section* ρ(0*yz*). The first-section ρ(0*yz*) calculated with mercury phase angles confirmed the impression that the sulphur is not at $z = 0$. It showed a much elongated peak (Fig. 2*a*) from which a parameter of $z \sim 0{\cdot}1$ could be inferred. This deduction was checked by calculating two additional electron-density distributions: ρ(0*yz*) in Fig. 2*b*

has phase angles calculated for mercury at $z = 0$ and sulphur at $z = 0{\cdot}10$; $\rho(0yz)$ in Fig. 2*c* has phase angles calculated for mercury at $z = 0$ and sulphur at $z = 0{\cdot}31$. Fig. 2*b* shows a single peak at $z = 0{\cdot}1$. Fig. 2*c* shows peaks both at the position used in the phase angle calculation and at $\pm z = 0{\cdot}1$.

The appearance of Fig. 2*a* and 2*c* has a close parallel in the effects of wrong phasing observed in other asymmetric syntheses, *e.g.*, in the hexacarboxylic acid of vitamin B_{12}.[1] Peaks about two-thirds of the expected height appear at wrongly assumed positions, and smaller peaks at the correct atom positions. The positions assumed here in Fig. 2*a* and 2*c* correspond to linear and tetrahedral S–Hg–S angles. It is clear that neither assumption is as satisfactory as that used in Fig. 2*b* where a single peak appears at $z = 0{\cdot}1$. This leads to an angle S–Hg–S of 155°.

FIG. 3. *Section, $\rho(5/120, y, 0)$, of the electron density. Contours at intervals of* 1 e Å^{-3}; *zero contour, broken line; negative contours, dotted lines.*



(*c*) *Three-dimensional electron-density series.* This was finally calculated, phased by mercury and sulphur in the position found above. It was expected that the phase angles would be sufficiently accurate to show the light-atom peaks clearly. But the electron-density maps are very confused; peaks range from 1 to 4½ e Å^{-3} in height and are distorted or spread over large areas. By using the projection, and known bond lengths, it was possible to place most of the atoms in regions of 2 e Å^{-3} or more, near or on peaks, but a few atoms are in regions of only 1 or 1½ e Å^{-3}. There are also many spurious peaks not corresponding to atomic positions. A typical section is shown in Fig. 3.

Approximate z co-ordinates had previously been found by arranging a model over the (001) Fourier projection, and were compared with those of the three-dimensional series. The tilt of the benzene ring C_2–C_7 was appreciably altered, and that of the ring C_8–C_{13} was slightly altered, with corresponding small changes in the –N–N– chain.

Diffraction effects around the mercury atom are serious, and the incompleteness of the data limits the possible accuracy of the series. But the incompleteness of the phasing and the false symmetry also contribute to the confusion in the electron-density maps. The importance of a heavy atom in determining the scattered intensities depends on the ratio $f^2_{\text{heavy atom}}/\sum f^2_{\text{all atoms}}$ (equal to 0·735 here), and so should its effectiveness in phasing a Fourier series. According to Luzzatti,[2] who gives the light-atom peaks to be expected in a three-dimensional Fourier series as a function of this ratio, the carbon and nitrogen peaks in mercury dithizone should be 3·5 and 4·1 e Å^{-3} respectively; many of them are found in the range 3—4 e Å^{-3}. The difficulty in interpretation arises not because the peaks are too low, but because of the many distortions and spurious peaks.

The partial false symmetry is introduced by using phase angles based on atoms in or

[1] Pickworth, D.Phil. Thesis, Oxford, 1955, p. 68.
[2] Luzzatti, *Acta Cryst.*, 1953, **6**, 142.

near special positions. If all the phases used were derived from the positions Hg at 0,0,0; S at 0,y,0, there would be centres of symmetry at $\frac{1}{8},\frac{1}{8},\frac{1}{8}$, and $\frac{1}{8},\frac{1}{8},\frac{5}{8}$, etc. The phases used for F($hk1$), F($hk2$), and F($hk3$) are derived from Hg at 0,0,0; S at 0,y,0·1, and so are

FIG. 4. *The atomic arrangement in projection down the* c*-axis.*

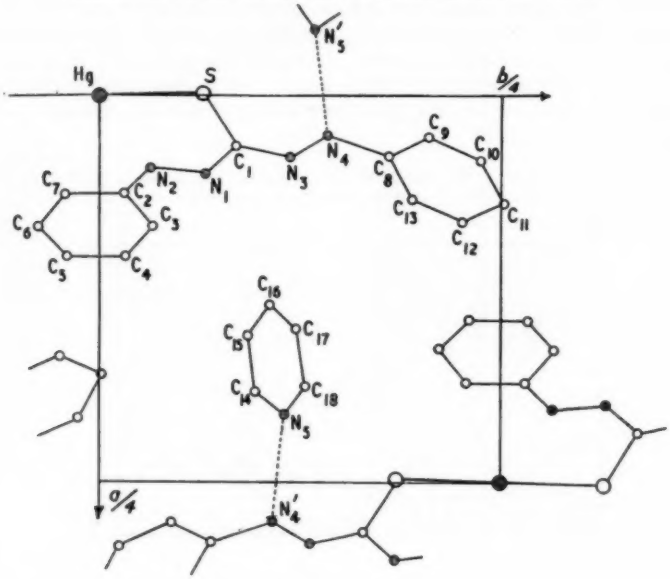
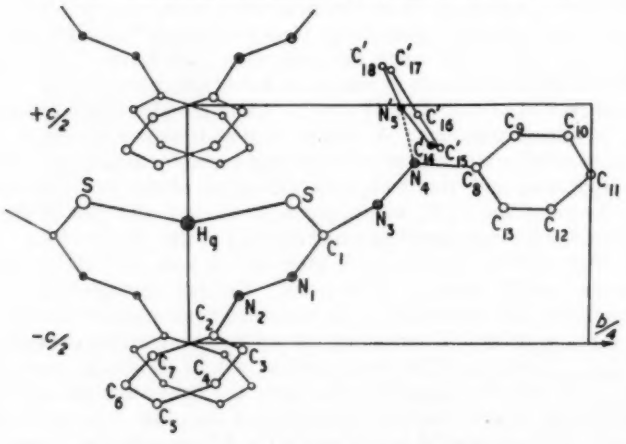


FIG. 5. *The atomic arrangement in projection down the* a*-axis.*



nearly centrosymmetric. But the *signs* used for F($hk0$), with no mercury contributions, are derived from the known atomic positions in projection and do not give these centres of symmetry. The extra symmetry is obvious when appropriate Fourier sections are compared; for instance, the large spurious peak in the section in Fig. 3 is related to N_5 in the pyridine molecule.

Further work on the three-dimensional data is not being carried out at present, but may be considered later when more computing facilities are available. No doubt the appearance of the three-dimensional electron-density series could be greatly improved by using phase angles, including the light-atom positions, but even then, no great accuracy in interatomic distances would be expected.

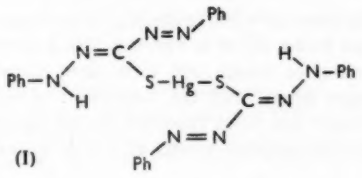
Description of the Structure and Discussion.

The atomic arrangement is shown in Figs. 4 and 5, and the atomic co-ordinates are given in Table 2. The co-ordinates of the sulphur atom are probably accurate to $\pm 0{\cdot}04$ Å; those of carbon and nitrogen atoms are much more approximate.

Table 2. *Fractional atomic co-ordinates.*

	x	y	z		x	y	z		x	y	z
Hg	0	0	0	C_8	0·038	0·180	0·24	N_1	0·050	0·066	0·78
S	0·247	0·185	0·345	C_9	0·026	0·203	0·37	N_2	0·045	0·033	0·70
C_1	0·033	0·084	0·95	C_{10}	0·042	0·237	0·36	N_3	0·040	0·118	0·085
C_2	0·064	0·016	0·525	C_{11}	0·183	0·001	0·97	N_4	0·025	0·124	0·25
C_3	0·087	0·034	0·475	C_{12}	0·082	0·227	0·06				
C_4	0·103	0·017	0·32	C_{13}	0·067	0·196	0·07	C_{14}	0·192	0·098	0·595
C_5	0·147	0·230	0·50					C_{15}	0·163	0·092	0·575
C_6	0·166	0·212	0·565					C_{16}	0·134	0·105	0·71
C_7	0·187	0·228	0·70					C_{17}	0·150	0·123	0·90
								C_{18}	0·188	0·128	0·92
								N_5	0·207	0·116	0·75

The primary bonding of dithizone to mercury is through the sulphur atom, but a nitrogen atom of the azo-group is also weakly co-ordinated to the mercury. The dithizone group is in an extended form, with no possibility of internal hydrogen bonding. The molecule can be written as in (I). There is probably a hydrogen bond between the NH group (N_4) and the pyridine nitrogen (N_5); the distance N_4–N_5 is less than 3 Å, but the atoms $C_{16} \ldots N_5 \ldots N_4$ depart considerably from a straight line.



(I)

The packing arrangement is shown in Fig. 6. The space which the pyridine molecules occupy is like a channel parallel to the c-axis; this should account for the easy loss of pyridine from the crystals in air. The highest measured density corresponds to 75% of the theoretical pyridine content in $Hg(C_{13}H_{11}N_4S)_2,2C_5H_5N$, but some pyridine would almost certainly be lost in the density measurement in an aqueous solution.

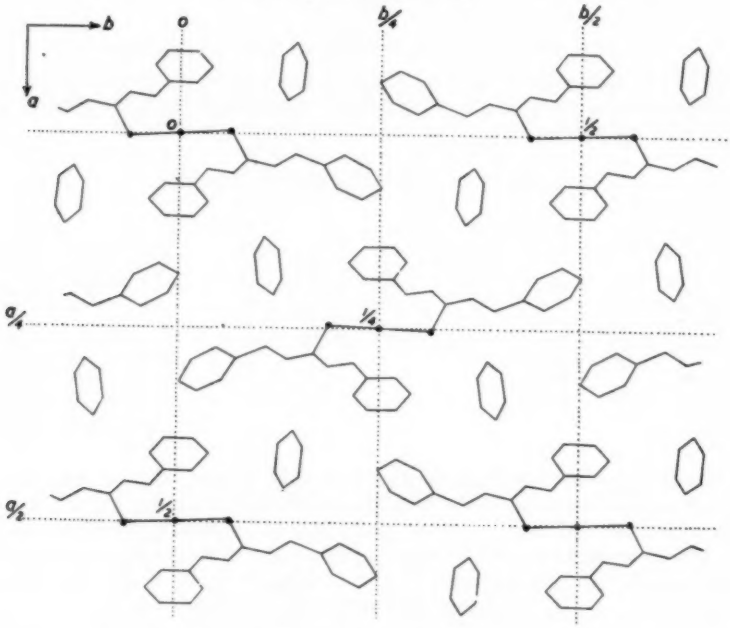
Probably all metal dithizones are similarly bonded through sulphur with nitrogen co-ordination; a more nearly tetrahedral arrangement around the metal atom would seem likely with other metals, especially those with smaller atomic radius. Crystalline zinc dithizone has been obtained but is not isomorphous with mercury dithizone. [It is possible, of course, that in the dithizones of cobalt, nickel, zinc, etc., metal–nitrogen bonding might be favoured, just as in the series of complex thiocyanates, $K_2M(SCN)_4$, when M is Zn, Cr, or Co there is metal–nitrogen bonding, but when M is Rh, Ag, Cd, or Pt, there is metal–sulphur bonding.[3]]

A most interesting feature of the structure is the co-ordination group around mercury,

[3] Zhdanov and Zvonkova, 13th Conference, I.U.P.A.C., 1953 (Stockholm), p. 153.

shown in Fig. 7. The Hg–S bond length, $2{\cdot}4_1$ Å, is normal for a covalent bond, but the Hg–N distance, 2·5—2·6 Å, and the angle, S–Hg–S, of 155° are quite unusual. Even

FIG. 6. *Projection down the* c*-axis showing the packing of molecules.* (*The* z*-co-ordinates of the mercury atoms are shown.*)



after allowance for a possible error of 0·2 Å in the Hg–N distance, it is significantly different from either a covalent bond (~2·1 Å) or a van der Waals contact. The arrangement is best described as a distortion of linear (*sp*) bicovalent mercury, S–Hg–S, due to the approach of the two nitrogen atoms and the formation of weak, secondary, Hg . . . . N bonds. A similar arrangement has been reported in one other compound, $KHg(SCN)_3$.[4] Here mercury is bonded to two sulphur atoms at 2·4 Å, making an angle at mercury of

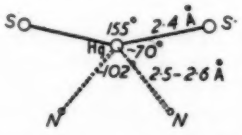


FIG. 7. *The co-ordination group around the mercury atom.*

approximately 155°; two more sulphur atoms, at about 2·8 Å, complete a very distorted tetrahedron.

A survey of mercury compounds (other than regular tetrahedral ones) shows that small deviations from linearity frequently occur. Also, many mercury derivatives, such as diphenylmercury, have appreciable dipole moments in benzene and other organic solvents, corresponding to bond angles in the region of 150°—presumably with some solvation.[5] All this evidence suggests that deviation from linearity does not greatly affect the energy of –X–Hg–X–; therefore when, by such deviation, additional weak bond formation becomes possible, the energy change is favourable.

[4] Zhdanov and Sanadse, *Zhur. Fiz. Khim.*, 1952, **26**, 469.
[5] Kadomtzeff, *Compt. rend.*, 1949, **228**, 681.

Experimental

Preparation of Crystals.—Mercury dithizone was prepared as described by Irving *et al.*[6] and deep red needles were obtained by crystallisation from aqueous pyridine. They deteriorated slowly in air, probably by loss of solvent. They were not analysed, because the analysis of crystals, dried (and therefore containing no pyridine), was reported by Irving *et al.* and was satisfactory.

Preliminary Data.—Oscillation photographs and Weissenberg photographs about the needle axis were taken. The cell dimensions were determined from Weissenberg photographs, calibrated with copper powder lines. Only the reflections hkl, with $h + k = 2n$, $k + l = 2n$; $0kl$, with $k = 4n$; and $h0l$, with $h = 4n$, were observed, so the space group is $Fdd2$. In this space group there are 16 general equivalent positions. The eight mercury atoms must be in the special positions on the two-fold axes. It was observed that, in addition to the above space-group absences, nearly all the reflections $hk0$, $hk2$, with $h + k + l = 4n + 2$, are either weak or absent, showing again that the mercury atoms lie on the two-fold axes. The z parameter of one can be arbitrarily chosen as zero, so the mercury positions are 0,0,0; $\frac{1}{4},\frac{1}{4},\frac{1}{4}$; etc.

The density data are given on p. 4136.

Intensity Measurements.—Weissenberg photographs on multiple films were taken, with Cu-K_α radiation, for the layers $hk0$, $hk1$, $hk2$, and $hk3$. Because of deterioration of the crystals a fresh one was required for each layer. The intensities were measured visually, and Lorentz and polarisation corrections applied. Reflections with $\sin\theta/\lambda \geqslant 0{\cdot}5$ were observed on some photographs but were rather weak for satisfactory measurement.

Absorption Corrections.—The linear absorption coefficient is 112 cm.$^{-1}$. The rotation axis of the crystals in all the Weissenberg photographs was parallel to the needle axis, c, and the cross-section was roughly square with sides about 0·04 mm. Absorption corrections were estimated for 70 of the $hk0$ reflections by a graphical method, based on that of Albrecht.[7] It was found that, provided the cross-section of each crystal used was approximately square, and the sides less than *ca.* 1 mm., no correction need be made.

Scale and Temperature Factors.—The temperature factor was determined by Wilson's method,[8] and $B = 2{\cdot}7_6$ Å^2 was found. The atomic scattering factors used were: for carbon and nitrogen, those of Macgillavry;[9] for hydrogen, that of McWeeney;[10] and for mercury, that of James and Brindley.[11] (The work was done before Thomas and Umeda's mercury scattering factor[12] was published.) The absolute scale factor cannot be determined by Wilson's method here, on account of the mercury atoms in special positions; it was determined by a comparison of observed and calculated structure factors. Later the scale and temperature factors were checked by plotting $\log \langle F_{obs.}(hk0)/|F_{calc.}(hk0)|\rangle_s$ against $\sin^2\theta/\lambda^2$, (where $\langle\ \rangle_s$ signifies an average over a range of $\sin^2\theta$ values); no change in B greater than 0·1 Å^2 was indicated.

Calculation of the Fourier Projections and Sections, and of Structure Factors.—All these summations were done by punched card methods on Hollerith machines. In the [001] projection, which is centrosymmetric, there were 135 terms whose signs were determined by mercury, and 23 to which the mercury does not contribute. In the refinement the series $(F_{obs.} - F_{Hg})$ was used.

In the generalised projections the components $C_L(xy)$ and $S_L(xy)$ of $\rho_L(xy)$ were calculated, mercury phases being used.

Phase angles for the three-dimensional series were calculated by hand; the assumption can be made that $x_s = 0$ (or 0·25), which makes the phase angle independent of h.

The three-dimensional Fourier series was calculated on " Deuce " at the National Physical Laboratory, the phases calculated for the sections above being used. Because these are independent of h, it was possible to use a simplified form of the electron-density expression.

I thank Mrs. D. M. Hodgkin for help and encouragement; also Dr. H. M. N. Irving for suggesting the problem, and Dr. J. S. Rollett for the Fourier calculation on " Deuce."

Chemical Crystallography Laboratory,
South Parks Road, Oxford. [*Received, June 2nd*, 1958.]

[6] Irving, Andrew, and Risdon, *J.*, 1949, 541.
[7] Albrecht, *Rev. Sci. Instr.*, 1939, **10**, 221.
[8] Wilson, *Nature*, 1942, **150**, 152.
[9] Macgillavry, *Acta Cryst.*, 1955, **8**, 478.
[10] McWeeney, *ibid.*, 1951, **4**, 513.
[11] Internationale Tabellen zur Bestimmung von Kristallstrukturen, Berlin, 1935.
[12] Thomas and Umeda, *J. Chem. Phys.*, 1957, **26**, 293.

834. *Thermodynamics of Ion Association. Part V.* Dissociation of the Bisulphate Ion.*

By V. S. K. Nair and G. H. Nancollas.

The thermodynamic dissociation constant of the bisulphate ion, as redetermined by a precision e.m.f. method between 0° and 45°, is compared with those by other workers, and the derived heat of dissociation, $\Delta H = -5{\cdot}6 \pm 0{\cdot}2$ kcal./mole, is in good agreement with the calorimetric value.

The extension of our thermodynamic study [1] of the formation of ion pairs between univalent ions of opposite sign to similarly charged ions of higher valency type, such as sulphates of bivalent cations, requires a reliable value for the second dissociation constant of sulphuric acid. The cell employed was similar to that used by Davies, Jones, and Monk [2]

$$H_2,Pt \mid HCl, H_2SO_4 \mid AgCl\text{–}Ag$$

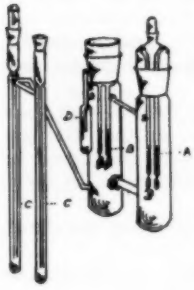
who obtained e.m.f.s to within ± 100 μv. Using a more refined apparatus and different cell design, we were able to make measurements at lower ionic strengths, and e.m.f.s were determined to within ± 15 μv from 0° to 45°.

Experimental

Solutions were made up by weight with conductivity water prepared by mixed-bed deionisation.[3]

Constant-boiling hydrochloric acid was prepared by distillation of the "AnalaR" acid diluted to a specific gravity of 1·14, recommended modifications being introduced.[4,5,6] Concentrations were determined by estimating the chloride gravimetrically as silver chloride;[7] these agreed to within $\pm 0{\cdot}01\%$ and were within $\pm 0{\cdot}01\%$ of the theoretical concentration. Sulphuric acid solutions were made by dilution of three different samples of "AnalaR" acid; duplicate sulphate determinations as barium sulphate [7] agreed to $\pm 0{\cdot}02\%$.

The e.m.f. cell.



The e.m.f. cell (Figure) was of the conventional H pattern, similar to that used by Noyes and Ellis.[8] Two hydrogen pre-saturators, *C*, were made integral with the hydrogen-electrode compartment, as recommended by Harned and Morrison,[9] and the modifications of Ashby, Crook, and Datta [10] were also incorporated. The electrodes were supported in the compartments with standard ground-glass cones and each cell contained a pair of silver–silver chloride, *A*, and hydrogen electrodes, *B*, enabling four estimates of e.m.f. to be made. A guard tube, *D*, was fitted to the hydrogen electrode compartment and any liquid collecting in it was immediately removed.

Hydrogen electrodes consisted of stout platinum foil (0·4 × 2·5 cm.) welded to platinum wire (0·05 cm. diam.). A very thin coat of platinum black was deposited on them by electrolysis at about 0·2 a/cm.^{2} for 2 min. in 2·5% of chloroplatinic acid in N-hydrochloric acid, the current being reversed every 15 sec. The platinum black was removed with aqua regia after every alternate run and a fresh deposit

* Part IV, *J.*, 1958, 3706.

[1] Nair and Nancollas, *J.*, 1957, 318.
[2] Davies, Jones, and Monk, *Trans. Faraday Soc.*, 1951, **48**, 921.
[3] Davies and Nancollas, *Chem. and Ind.*, 1950, **7**, 129.
[4] Foulk and Hollingworth, *J. Amer. Chem. Soc.*, 1923, **45**, 1223.
[5] Titus and Smith, *ibid.*, 1941, **63**, 3266.
[6] Shaw, *Ind. Eng. Chem.*, 1926, **18**, 1065.
[7] Vogel, "A Text Book of Quantitative Analysis," Longmans, London, 1947.
[8] Noyes and Ellis, *J. Amer. Chem. Soc.*, 1917, **39**, 2532.
[9] Harned and Morrison, *Amer. J. Science*, 1937, **33**, 161.
[10] Ashby, Crook, and Datta, *Biochem. J.*, 1954, **56**, 190.

made. Electrodes were stored in conductivity water saturated with hydrogen. Spectroscopically pure silver oxide (Johnson Matthey & Co.) was used in the preparation of silver–silver chloride electrodes which were of the thermal electrolytic type incorporating at least 150—200 mg. of silver as recommended by Bates.[12] They were warmed in water at 50° for 2 hr. after chloridising [10] and stored in darkness in dilute, oxygen-free potassium chloride solution. Good platinum–Pyrex seals were ensured with all electrodes by casting a little Araldite resin in the bottom of the electrode tubes.

Cylinder hydrogen was freed from oxygen by passing through a " deoxo " purifier (Baker Platinum Division, Engelhard Industries Ltd., London) and saturated with water vapour in a series of bubblers. Solutions were bubbled with hydrogen for at least 1 hr. before use. Electrodes were washed three times with solution in a washing apparatus in which provision was made for hydrogen bubbling; they were then quickly transferred to the cell which was swept out with hydrogen. Filling was carried out in an all-glass apparatus by means of hydrogen pressure; the cells were placed in a thermostat, and a steady slow stream of hydrogen was maintained in the hydrogen electrode compartment. The thermostat could be maintained at any temperature between 0° and 45° to within ±0·005°. Temperatures were measured with platinum resistance thermometers, constructed as suggested by Barber,[13] and calibrated at the triple point of water and at several other temperatures below 100° against a resistance thermometer kindly lent by Dr. S. P. Datta which had an N.P.L. standardisation. Barber and Herington's [14] procedure was followed in constructing triple-point cells and in water purification. Thermometers were connected in series with a standard 25 ohm resistance maintained at 25° and a current of 1 mA was passed, the potential drop being measured with a vernier potentiometer. In order that e.m.f. measurements could be made at " round " temperatures a series of Beckmann thermometers to be used in the thermostat were calibrated with the resistance thermometers and were frequently checked.

E.m.f.s were measured with a precision vernier potentiometer (Type P.10., Croydon Precision Instrument Co.) in the range with direct reading to 10 μv. Further subdivision could be made from the deflection of the sensitive moving coil galvanometer (Type 41127, Cambridge Instrument Co.) used as a null detector with lamp and scale at 1 metre. Two Weston standard cells (Cambridge Instrument Co.) were kept permanently at 25° in an oil thermostat; their e.m.f. never differed by more than 20 μv.

Four cells could be accommodated in the thermostat and they required 3—4 hr. to come to equilibrium initially. Thereafter the e.m.f. remained constant to within 10 μv for more than ½ hr. and different combinations of electrodes agreed to within 20 μv. At subsequent temperatures the cells reached equilibrium within 1 hr. Observed e.m.f.s were corrected for pressure after adjusting barometer readings for latitude and temperature.

Results and Discussion

The standard potential of the silver–silver chloride electrode may vary [15] by as much as 200 μv, probably owing to small differences in the structure of the solid phases. Since the mean activity coefficient, $\gamma_{\pm}$, of 0·01 molal hydrochloric acid is uncertain only to about 0·0005, which corresponds to 30 μv, each electrode was standardised in this solution and the recommended $\gamma_{\pm}$ values [15] employed to calculate E°: $\gamma_{\pm} = 0{\cdot}908$ at 0° and 0·904 at 25°. At other temperatures, $\gamma_{\pm}$ values were obtained from [16]

$$\log \gamma_{\pm} = Am^{\frac{1}{2}}/(1 + m^{\frac{1}{2}}) + 0{\cdot}234m$$

which, with use of the appropriate values of the Debye–Hückel constant A, gives the same $\gamma_{\pm}$ values at 0° and 25° when $m = 0{\cdot}01$m. The E° values of different sets of electrodes never differed from Harned and Ehlers's values [17] by more than 230 μv. Purlee and

[11] Harned, *J. Amer. Chem. Soc.*, 1929, **51**, 416.
[12] Bates, " Electrometric pH Determinations," Wiley, New York, 1954, p. 200.
[13] Barber, *J. Sci. Instr.*, 1950, **27**, 47.
[14] Barber and Herington, *J. Appl. Phys.*, 1954, **5**, 41.
[15] Bates, Guggenheim, Harned, Ives, Janz, Monk, Robinson, Stokes, and Wynne-Jones, *J. Chem. Phys.*, 1956, **25**, 361.
[16] Guggenheim and Prue, *Trans. Faraday Soc.*, 1954, **50**, 231.
[17] Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350; 1933, **55**, 2179.

XUM

Grunwald [18] observed similar differences with silver–silver chloride electrodes formed either by chloridising silver mirrors or thermoelectrolytically.

The e.m.f. of the cell

$$H_2,Pt \mid HCl(m_1),\ H_2SO_4(m_2) \mid AgCl\text{–}Ag$$

may be written

$$E = E^\circ - k \log a_{H^+}a_{Cl^-}$$

or

$$-\log m_{H^+} = (E - E^\circ)/k + \log m_1 + 2 \log \gamma_\pm$$

where $k = 2{\cdot}3026RT/F$ and has the values given by Robinson and Stokes,[19] and m_1 and m_2 represent molal concentrations. The ionic strength

$$I = 2m_{H^+} - (m_1 + m_2)$$

$$m_{HSO_4^-} = m_1 + 2m_2 - m_{H^+}$$

and

$$m_{SO_4^{2-}} = m_2 - m_{HSO_4^-}$$

Activity coefficients were obtained from [20]

$$-\log \gamma_z = Az^2 [I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}}) - 0{\cdot}2I]$$

A being the Debye–Hückel constant, (kg./mole)$^{\frac{1}{2}}$, at the appropriate temperature.[21]

The thermodynamic dissociation constant $k_2 = m_{H^+}m_{SO_4^{2-}}\gamma_2/m_{HSO_4^-}$ was obtained by successive approximations of I and the results are given in Table 1.

The k_2 values are compared with those of Davies, Jones, and Monk [2] in Table 2. The differences between them may be accounted for almost completely by the use of the same A values in the calculations. The value at 25° of Davies, Jones, and Monk is based on $A = 0{\cdot}50$. Substitution of the Debye–Hückel value, 0·5085, brings k_2 into agreement with the present work. Recalculated values from Davies, Jones, and Monk's data are shown in Table 2.

At 25° there are many k_2 data, many of which have been reviewed elsewhere.[19] Hamer,[22] studying the cell $H_2,Pt \mid Na_2SO_4, NaHSO_4, NaCl \mid AgCl\text{–}Ag$, obtained a value of 0·0120; the data have been recalculated [2] with allowance for the formation of $NaSO_4^-$ ions to give $k_2 = 0{\cdot}0102$. Hamer [23] has re-examined the e.m.f. data using different values of ion-size parameter, a_i, and extrapolating to infinite dilution and has suggested that the k_2 values from the acid–acid cell [2] converge to a single value whereas his original data do not. This extrapolation procedure is open to objection, however, since it produces impossible β values in the activity-coefficient expression:

$$-\log \gamma_z = Az^2I^{\frac{1}{2}}/(1 + Ba_iI^{\frac{1}{2}}) + \beta I$$

The spectrophotometric value [24] ($k_2 = 0{\cdot}0104 \pm 0{\cdot}0003$) is usually regarded [19] as the most reliable. It is based, however, on a method which neglects the formation of $NaSO_4^-$ in sodium sulphate solutions and, moreover, a negative value for the ion size ($a_i = -5{\cdot}8$ Å) was apparently used.[23] Kerker [25] has recalculated conductance and transference-number data by the method of Sherrill and Noyes,[1] who obtained originally $k_2 = 0{\cdot}0118$,[26] and

[18] Purlee and Grunwald, *J. Phys. Chem.*, 1955, **59**, 1112.
[19] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955.
[20] Davies, *J.*, 1938, 2093.
[21] Manor, Bates, Hamer, and Acree, *J. Amer. Chem. Soc.*, 1943, **65**, 1765.
[22] Hamer, *J. Amer. Chem. Soc.*, 1934, **56**, 860.
[23] Hamer, Symposium on Structure of Electrolyte Solutions, Electrochem. Soc., Washington, May 1953; personal communication.
[24] Young, Klotz, and Singleterry, based on dissertations of the last two; University of Chicago, 1940, quoted in ref. 19.
[25] Kerker, *J. Amer. Chem. Soc.*, 1957, **79**, 3664.
[26] Sherrill and Noyes, *ibid.*, 1926, **48**, 1861.

XUM

TABLE 1. *E.m.f. measurements.*

No.	10^3m_1	10^3m_2	No.	10^3m_1	10^3m_2	No.	10^3m_1	10^3m_2	No.	10^3m_1	10^3m_2
1	1·2711	1·3498	6	5·0645	3·6773	11	6·7748	5·4093	16	2·8003	3·1488
2	1·8441	1·8564	7	5·1554	5·5379	12	5·3530	7·1315	17	2·3264	2·2471
3	2·1606	2·2481	8	6·7047	3·8888	13	8·1637	8·4059	18	3·2284	2·6627
4	2·3804	2·0919	9	2·0278	2·0131	14	5·7665	10·1000	19	2·7147	2·7006
5	3·5560	2·9684	10	4·6073	5·4429	15	2·1500	1·7383	20	3·8725	4·1791

No.	$E - E^\circ$	10^3I	$10^3m_{H^+}$	$10^3m_{HSO_4^-}$	10^3k_2	No.	$E - E^\circ$	10^3I	$10^3m_{H^+}$	$10^3m_{HSO_4^-}$	10^3k_2
		Temp. 0°						Temp. 25° (*contd.*)			
1	0·29131	5·058	3·8394	0·1312	2·66	13	0·23092$_4$	25·040	20·826	4·1498	1·15
2	0·27541	6·941	5·3206	0·2362	2·60	14	0·23979	26·02	20·954	5·0454	1·12
3	0·26791	8·255	6·3320	0·3248	2·60	15	0·29734	6·485	5·1866	0·4400	1·09
4	0·26583	8·060	6·2660	0·2981	2·62	16	0·28032	10·131	8·0410	1·0570	1·05
5	0·24864	11·429	8·9764	0·5164	2·79	17	0·29126	7·788	6·1804	0·6415	1·07
						18	0·22760	9·543	7·7160	0·8378	1·12
		Temp. 5°						Temp. 35°			
6	0·23929	14·331	11·537	0·8825	2·28	2	0·31245	6·298	4·9995	0·5573	0·824
7	0·23366	18·813	14·753	1·4781	2·38	3	0·30418	7·396	5·9026	0·7543	0·806
8	0·22920	16·311	13·452	1·0300	2·27	9	0·30787	6·833	5·4371	0·6170	0·859
						17	0·30164	7·504	6·0393	0·7833	0·777
		Temp. 15°				18	0·28749	9·208	7·5994	1·0044	0·827
6	0·24843	13·842	11·292	1·1273	1·59	20	0·27490	12·830	10·441	1·7897	0·868
7	0·24280	17·909	14·301	1·9301	1·58						
8	0·23795	15·788	13·191	1·2914	1·61			Temp. 45°			
						1	0·34145	4·517	3·5690	0·4017	0·622
		Temp. 25°				2	0·32323	6·076	4·8881	0·6683	0·614
1	0·31904	4·769	3·6961	0·2754	1·07	3	0·31468	7·140	5·7742	0·8826	0·615
2	0·30179	6·503	5·1005	0·4553	1·11	9	0·31864	6·530	5·2854	0·7678	0·598
3	0·29371	7·677	6·0431	0·6137	1·11	17	0·31210	7·221	5·8975	0·9251	0·580
4	0·29146	8·724	5·9632	0·6009	1·03	18	0·29752	8·834	7·3625	1·1914	0·603
5	0·27280	10·510	8·5163	0·9765	1·13	19	0·30382	8·444	6·9296	1·1863	0·592
7	0·25193	17·144	13·9187	2·3125	1·14	20	0·28465	12·203	10·127	2·1033	0·622
9	0·29737	7·049	5·5441	0·5099	1·14						
10	0·25593	16·498	13·273	2·2204	1·14						
11	0·24276$_4$	18·300	15·244	2·3493	1·15						
12	0·24726$_6$	20·285	16·386	3·2300	1·12						

TABLE 2. *Values of k_2.*

	0°	5°	15°	25°	35°	45°
Davies, Jones, and Monk [3]	—	1·73	1·43	1·03	0·78	—
Recalculated	—	1·90	1·56	1·09	0·80	—
Present work	2·62	2·31	1·59	1·10	0·82	0·60

has derived a value of 0·0102. There is still some doubt, however, about the value to be used for the conductance of the sulphate ion in such calculations. Kentama [27] has reported a value of 0·0114 from solubility measurements with silver sulphate.

The heat of dissociation of the bisulphate ion has been obtained by the method of least squares from the good linear plot of log k_2 against T^{-1}. The heat and entropy values agree well with the calorimetric values of Pitzer [28] as shown in Table 3.

TABLE 3. *Thermodynamic properties.*

	ΔH (kcal./mole)	ΔG (kcal./mole)	ΔS (cal. deg.$^{-1}$ mole^{-1})
Pitzer [28]	$-5·2 \pm 0·5$	2·62	−26·3
Present work	$-5·6 \pm 0·2$	2·67	−27·7

We thank Dr. S. P. Datta (University College, London) for advice, Mr. J. Leslie for the construction of the cells, and, for this and Part IV, the University of Travancore for a scholarship (to V. S. K. N.).

THE UNIVERSITY, GLASGOW, W.2. [*Received, June 10th*, 1958.]

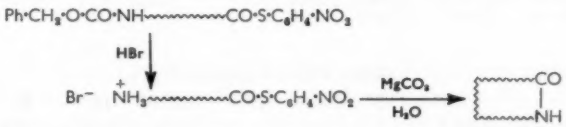
[27] Kentama, *Suomen Kem.*, 1957, **1**, 30.
[28] Pitzer, *J. Amer. Chem. Soc.*, 1937, **59**, 2365.

835. *Peptides. Part VIII.* Cyclic Peptides Derived from Leucine and Glycine.*

By G. W. Kenner, P. J. Thomson, and J. M. Turner.

The *p*-nitrophenyl thiolesters of benzyloxycarbonylpeptides can be converted into cyclic peptides by removal of the benzyloxycarbonyl group with hydrogen bromide and subsequent cyclisation in neutral aqueous solution. The derivative of glycyl-L-leucylglycine yields the cyclic hexapeptide, identical with that prepared from the derivative of glycyl-L-leucylglycylglycyl-L-leucylglycine. No cyclic peptide could be obtained from the derivatives of glycyl-L-leucylglycyl-L-leucine and L-leucylglycyl-L-leucylglycine, but cyclic pentapeptides were formed in good yield. The yield was significantly higher from the derivative of glycyl-L-leucylglycyl-D-leucylglycine than from the L-L-diastereoisomer, and this difference has been correlated with the lower dielectric increment of the open-chain L-D-pentapeptide.

Cyclic peptides, of which the best known is gramicidin-S, form a well-recognised class of natural product,[1] but until recently there were only scattered, and not always convincing, reports of synthetic cyclic peptides.[2] In seeking a general method of synthesis, we adopted a principle already employed † by Winitz and Fruton;[3] in a synthesis of this pattern, a terminal amino-protecting group is removed from a peptide derivative possessing an activated carbonyl grouping at the other end of the chain, and then cyclisation can follow. The activating group must be comparatively stable in order to survive the removal of the amino-protecting group and the wait for the relatively infrequent approach of the terminal amino-group. Consequently the *p*-nitrophenyl thiolesters, which are easily prepared from amino-protected peptides,[5] are suitable derivatives, although the esterified amino-acid residue should then be glycine in order to avoid the substantial risk of racemisation.[5]



These thiolesters withstand completely the treatment with hydrogen bromide in acetic acid for removal of benzyloxycarbonyl, which is thus a convenient amino-protecting group. This method, which is depicted above, was tried first with a pentapeptide because this has the smallest ring which should be formed easily. Since the preliminary announcement of the successful outcome,[6] Schwyzer and his colleagues have published work along somewhat similar lines [7] and this has culminated in the synthesis of gramicidin-S.[8] Their improved technique for isolating the cyclic peptides, by passage through ion-exchange columns, has been incorporated in the experiments recorded below.

The aspect of cyclisation in the peptide series which has chiefly interested us, once the method had been developed, has been its stereochemistry. It is generally recognised that in open-chain peptides the amide group prefers a planar conformation and that the conformation in which the " carbonyl "-oxygen and the " imino "-hydrogen are *trans*- is

* Part VII, *J.*, 1957, 1407.

† There is some doubt [4] whether the material described by them was actually a cyclic peptide.

[1] Bricas and Fromageot, *Adv. Protein Chem.*, 1953, **8**, 1.
[2] Goodman and Kenner, *ibid.*, 1957, **12**, 494.
[3] Winitz and Fruton, *J. Amer. Chem. Soc.*, 1953, **75**, 3041.
[4] Heyns, Walter, and Müller, *Angew. Chem.*, 1956, **68**, 617.
[5] Farrington, Hextall, Kenner, and Turner, *J.*, 1957, 1407.
[6] Kenner and Turner, *Chem. and Ind.*, 1955, 602.
[7] Schwyzer, Iselin, Rittel, and Sieber, *Helv. Chim. Acta*, 1956, **39**, 872.
[8] Schwyzer and Sieber, *ibid.*, 1957, **40**, 624.

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preferred to the other in which they are *cis*.[9] A natural presumption is that those cyclic peptides which can adopt conformations obeying these rules will be formed most easily, and, with the aid of molecular models particularly suitable for peptides,[10] it can be seen that five amino-acid residues are required by these conditions.* However dioxopiperazines, in which both amide groups are *cis*, are formed quite easily from many dipeptide esters, and therefore a small series of cyclisations was studied. For ease of handling, peptides with alternating glycine and L-leucine residues were chosen. A crystalline cyclic peptide was obtained from glycyl-L-leucylglycine *p*-nitrophenyl thiolester in more than 10% yield, but this was found to be the cyclic hexapeptide formed by junction of two units before cyclisation; it was identified with the substance produced by cyclisation of glycyl-L-leucylglycylglycyl-L-leucylglycine *p*-nitrophenyl thiolester. For determinations of molecular weight, the cyclic peptides were dissolved in trifluoroacetic acid and initially the apparatus of Morton, Campbell, and Ma [11] was used successfully for the isopiestic method. This technique was also used by Schwyzer and his colleagues,[7] but later we were unable to observe a steady state of equilibrium, possibly owing to a leakage of vapour. However, as no reactivity towards ninhydrin was generated from the cyclic peptides during half an hour in boiling trifluoroacetic acid, an ebullioscopic method [12] was a reliable alternative. Our failure to detect any cyclic tripeptide in the product from glycyl-L-leucylglycine *p*-nitrophenyl thiolester is not at all surprising because, even with three *cis*-amide groups, the molecular model is strained, mainly by the repulsion between one hydrogen atom on each of the methylene or methine groups. Formation of the same cyclic hexapeptide from derivatives of glycyl-L-leucylgylcine has been observed independently by Schwyzer, Sieber, and Gorup.[13] Similarly it has already been established [14] that the product [15] from glycylglycylglycine azide is *cyclo*hexaglycyl. On the other hand, *cyclo*glycylglycyl-DL-prolyl is formed gradually from gylcyl-DL-prolylglycine ethyl ester: [16] this may be regarded as an exceptional instance related to the pronounced tendency for formation of dioxopiperazines from derivatives of dipeptides containing proline.[17]

Our attempts to synthesise *cyclo*-L-leucylglycyl-L-leucylglycyl from either of the open-chain tetrapeptide *p*-nitrophenyl thiolesters were unsuccessful; traces of crystalline material were obtained but it was not characterised. Perhaps the most surprising feature of these results is the lack of the cyclic octapeptide; unfortunately the cyclisation of an octapeptide derivative has not been examined by us because our attempts to prepare the thiolester from benzyloxycarbonyl-L-leucylglycyl-L-leucylglycyl-L-leucylglycyl-L-leucylglycine were unsuccessful, presumably on account of its insolubility. It should be noted that the synthesis of *cyclo*tetraglycyl under different conditions is well authenticated.[7]

The cyclic pentapeptides were formed readily from glycyl-L-leucylglycyl-L-leucylglycine *p*-nitropheny thiolester and its L-D-diastereoisomer in yields of 41 and 57% respectively. Although the methods of isolation differed because the cyclic L-D-peptide separated immediately from the reaction mixture whereas the L-L-product remained in solution, we regard the difference as genuine and fundamentally significant. It might arise from reduced repulsion of the side-chains in the L-D-cyclic peptide, or rather the transition state leading to it; this effect has been invoked to account for the frequent occurrence of

* A model, which has planar *trans*-amide groups, of a cyclic tetrapeptide [7] can actually be assembled with some difficulty, but others in which one or more of the amide groups are *cis* are assembled much more easily.

[9] Pauling and Corey, *Fortschr. Chem. org. Naturstoffe*, 1954, **11**, 180.
[10] Hartley and Robinson, *Trans. Faraday Soc.*, 1952, **48**, 847.
[11] Morton, Campbell, and Ma, *Analyst*, 1953, **78**, 722.
[12] Wilson, *Analyst*, 1948, **73**, 585 (Sucharda–Bobranski apparatus).
[13] Schwyzer, Sieber, and Gorup, *Chimia*, 1958, **12**, 90.
[14] Sheehan, Goodman, and Richardson, *J. Amer. Chem. Soc.*, 1955, **77**, 6391; Bamford and Weymouth, *ibid.*, p. 6368.
[15] Sheehan and Richardson, *ibid.*, 1954, **76**, 6329.
[16] P. W. G. Smith, *J.*, 1957, 3985.
[17] E. L. Smith and Bergmann, *J. Biol. Chem.*, 1944, **153**, 627; Rydon and P. W. G. Smith, *J.*, 1956, 3642.

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D-amino-acid residues in natural cyclic peptides,[18] but the interaction of neighbouring residues seems to have been envisaged originally and in the present instance the effect is not obvious with molecular models. A second possibility, which would correspond to a change in the entropy instead of the enthalpy of activation, is that the conformation of the open-chain L-D-compound is more frequently close to that of the transition state. While the amide groups have rigidly the planar *trans*-conformation, this situation could be caused by preference for certain angles of rotation about some or all of the bonds between the asymmetric carbon atoms and the amide groups. Although experimental evidence has been lacking, such preferences in the peptide series have been discussed[19] and we accept this explanation as a useful hypothesis.

Independent evidence of the conformation of the related open-chain peptides is furnished by dielectric data. The contributions made by these dipolar ions to the dielectric constants of their aqueous solutions (the dielectric increments) are approximately proportional to the squares of their dipole moments. We find that the dielectric increment of glycyl-L-leucylglycyl-L-leucylglycine is 186 whereas that of the L-D-diastereoisomer is 169. The conclusion[20] from earlier work, which did not include studies of diastereoisomers, either that there is free rotation of the peptide chain or that several preferred conformations are equally probable is apparently unjustified, but confirmation and theoretical explanation will require more sets of comparable data. We hope that greater differences will be encountered with more carefully selected diastereoisomers: the pair already studied was chosen for ease of manufacture and isolation of the cyclic peptides.

The difference between the dielectric increments of the diastereoisomeric pentapeptides is in the direction predicted by our hypothesis, but it might be considered too small to account for the difference in the yields of cyclic peptides. However, it must be realised that the ease of cyclisation will be determined by the contribution of only the conformations with smaller dipole moments and, therefore, although the two phenomena should vary in the same direction, close correspondence is not to be expected. Further it may not be legitimate to equate the free peptide with its thiolester.

Experimental

M. p.s are corrected. Evaporations were carried out under reduced pressure.

*Tri-*p*-nitrophenyl Phosphorotrithioite.*—Method (a) described in Part VII [5] was modified for work on a larger scale. A solution of lithium (2·21 g.) in methanol (100 c.c.) was mixed with a solution of *p*-nitrothiophenol (49·3 g.; prepared from either *p*-chloronitrobenzene [21] or bis-*p*-nitrophenyl disulphide [22]) in dimethylformamide (180 c.c.). The reaction with phosphorus trichloride (9·6 c.c.) was carried out as before, and the crude product was washed with dimethylformamide (10 c.c.) and ethylene dichloride (10 c.c.) before being recrystallised from ethylene dichloride, which did not dissolve a minor impurity. The yield of recrystallised phosphorotrithioite was 30 g. (55%).

*Benzyloxycarbonyl-*D*-leucylglycine.*—The same sequence of operations as in the L-series [5] led through *benzyloxycarbonyl-*D*-leucine* p-*nitrophenyl thiolester*, m. p. 106—107° (Found: C, 60·0; H, 5·6. $C_{20}H_{22}O_5N_2S$ requires C, 59·7; H, 5·5; N, 7·0%), to *benzyloxycarbonyl-*D*-leucylglycine*, m. p. 116—117°, $[\alpha]_D^{22}$ +25·9° (*c* 2 in EtOH) (Found: C, 59·2; H, 7·0; N, 8·8. $C_{16}H_{22}O_5N_2$ requires C, 59·6; H, 6·9; N, 8·7%).

*Benzyloxycarbonyl-*DL*-leucylglycine.*—This *compound*, m. p. 162° (Found: C, 59·3; H, 6·6; N, 8·9%), was likewise prepared through *benzyloxycarbonyl-*DL*-leucine* p-*nitrolphenyl thiolester*, m. p. 98° (Found: C, 60·0; H, 5·2; N, 7·3%).

*Benzyloxycarbonylglycyl-*L*-leucylglycyl-*D*-leucylglycine* p-*Nitrophenyl thiolester.*—Benzyloxycarbonyl-D-leucylglycine was treated with hydrogen bromide in acetic acid and then coupled

[18] Neuberger, *Adv. Protein Chem.*, 1948, **4**, 372.
[19] Pauling and Corey, *Proc. Nat. Acad. Sci. U.S.A.*, 1951, **37**, 729; Mizushima, *Adv. Protein Chem.*, 1954, **9**, 316.
[20] Cohn and Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publ. Inc., New York, 1943, p. 152—154.
[21] Shirley, "Preparation of Organic Intermediates," Wiley, New York, 1951, p. 237.
[22] Zincke, *Annalen*, 1913, **400**, 1.

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with benzyloxycarbonylglycyl-L-leucylglycine *p*-nitrophenyl thiolester, as in the preparation of benzyloxycarbonylglycyl-L-leucylglycyl-L-leucylglycine,[5] which has $[\alpha]_D^{27}$ −22·0° (*c* 2 in EtOH). The L-D-diastereoisomer was obtained as a resinous solid with $[\alpha]_D^{27}$ −4·0° (*c* 4·5 in EtOH), and it was converted by procedure (a) [5] into the p-*nitrophenyl thiolester*, a colourless amorphous powder having m. p. 150—152° after repeated precipitation by water from acetone (Found: C, 55·7; H, 6·5; N, 12·0. $C_{32}H_{42}O_9N_6S$ requires C, 56·0; H, 6·2; N, 12·2%).

Benzyloxycarbonylglycyl-L-leucylglycylglycyl-L-leucylglycine p-*Nitrophenyl Thiolester*.—The preparation of this *hexapeptide derivative* from benzyloxycarbonylglycyl-L-leucylglycine was analogous to that of the foregoing pentapeptide derivative. It was obtained as a colourless amorphous powder, m. p. 194—195°, after precipitation by ether from methanol (Found: C, 54·8; H, 5·8. $C_{34}H_{45}O_{10}N_7S$ requires C, 54·9; H, 6·1%).

cyclo*Glycyl-L-leucylglycyl-L-leucylglycyl*.—Benzyloxycarbonylglycyl-L-leucylglycyl-L-leucylglycine *p*-nitrophenyl thiolester [5] (0·686 g.) was shaken with acetic acid (3·5 c.c.) and 6N-hydrogen bromide in acetic acid (1 c.c.) until it had dissolved (1 hr.); the solution was then evaporated under nitrogen (1 mm.). The residue was thoroughly triturated with ether (50 c.c.) before being partitioned between water (50 c.c.) and ethyl acetate (30 c.c.), which was washed with water (15 c.c.). The material recovered by evaporation of the dried ethyl acetate was subjected to a second treatment with hydrogen bromide and subsequent separation. The combined aqueous solutions were added during 6 hr. (approximately 1 drop every 10 sec.) to a stirred suspension of magnesium carbonate (0·80 g.) in water (200 c.c.). Stirring was continued overnight and then 30% hydrogen peroxide (3 drops) was added. Filtration removed the excess of magnesium carbonate and the bis-*p*-nitrophenyl disulphide; a check that cyclic peptide did not remain in the solid was made by exhaustive extraction with hot 95% ethanol after the disulphide had been removed in boiling ethyl acetate (30 c.c.). The aqueous filtrate was passed successively through columns of Dowex-50 (hydrogen form; 50 g.) and Dowex-2 (hydroxide form; 50 g.) ion-exchange resins. The *cyclic peptide* (0·161 g., 41%) was obtained on concentration of the effluent in two crops of needles, decomp. 290—300°; recrystallised from 95% ethanol, it had $[\alpha]_D^{20}$ −8·7° (*c* 3 in trifluoroacetic acid) [Found: C, 54·4; H, 7·7; N, 17·6%; *M*, 389 (isopiestic [11]), 389 (ebullioscopic [12]). $C_{18}H_{31}O_5N_5$ requires C, 54·4; H, 7·9; N, 17·6%; *M*, 397]. Its infrared absorption had maxima at 3260, 3070, 2950, 2870, 1651 (s), 1537 (s), 1473, 1457, 1431, 1408, 1371, 1340, 1321, 1292, 1243, 1224, 1197, 1157, 1133, 1095, 1077, 1030, 1006, 963, 940, 877, and 852 cm.$^{-1}$ (mulls in Nujol of hexachlorobutadiene), or at 3279 (s), 3077, 2950, 2865, 1664 (s), 1546 (s), 1460, 1427, 1406, 1383, 1370, 1323, 1287, 1242, 1196, 1170, 1156, 1130, 1031, 1006, 966, 940, 922, 878, 852, 830 cm.$^{-1}$ (KBr disc).

Similar yields (between 38 and 44%) were obtained on several repetitions and also by an earlier technique in which the hydrobromide solution was added in one portion to an aqueous suspension of magnesium oxide (1 g. in 4 l. of water when starting with 0·2 g. of benzyloxycarbonylpeptide thiolester) and the product was isolated by countercurrent distribution; further details were given in our preliminary communication.[6] Satisfactory cyclisation of the phenyl thiolester (lacking the nitro-group) was achieved by treating its hydrobromide with potassium *tert.*-butoxide in boiling *tert.*-butyl alcohol during 48 hr.

cyclo*Glycyl-L-leucylglycyl-D-leucylglycyl*.—Treatment of benzyloxycarbonylglycyl-L-leucylglycyl-D-leucylglycine *p*-nitrophenyl thiolester with hydrogen bromide and cyclisation were carried out as in the foregoing experiment; during addition of the aqueous solution to the suspension of magnesium carbonate, a flocculent material precipitated and frothing occurred. After 30% hydrogen peroxide (3 drops) had been added, the mixture was neutralised with 10N-hydrochloric acid (0·7 c.c.) and filtered. Evaporation of the solution after passage through cation- and anion-exchange columns did not leave any product, but the insoluble *cyclic peptide* (0·217 g., 55%; on repetition, 0·235 g., 59%) remained when the solid was exhaustively extracted with boiling ethyl acetate. Being insoluble in hot water, hot methanol, concentrated hydrochloric acid, dilute aqueous sodium hydroxide, glacial acetic acid, and dimethylformamide, it was purified by precipitation with ether from trifluoroacetic acid, and formed a colourless amorphous powder, decomp. 300—310° [Found: C, 54·0; H, 8·1; N, 17·7%; *M* (ebullioscopic [12]), 376]. Its infrared absorption (mulls in Nujol or hexachlorobutadiene) had maxima at 3280, 3065, 2950, 1661 (s), 1643 (s), 1548 (s), 1473, 1423, 1390, 1377, 1327, 1295, 1277, 1242, 1215, 1173, 1147, 1087, 1020, 917, 851, and 787 cm.$^{-1}$.

cyclo*Glycyl-L-leucylglycylglycyl-L-leucylglycyl*.—(*a*) After treatment of benzyloxycarbonylglycyl-L-leucylglycylglycyl-L-leucylglycine *p*-nitrophenyl thiolester (0·700 g.) with hydrogen

bromide in acetic acid, cyclisation and isolation followed the same course as with the L-L-pentapeptide derivative. The crystalline *cyclic peptide* was obtained directly in two crops (total 0·095 g.) on concentration of the effluent from the second ion-exchange column; it was recrystallised from methanol–ether in prisms (0·087 g., 20%), decomp. 310—320° [Found: C, 53·0; H, 7·6; N, 18·8%; *M* (ebullioscopic [12]), 444. $C_{29}H_{34}O_6N_6$ requires C, 52·9; H, 7·5; N, 18·6%; *M*, 454]. Its infrared absorption (mulls in Nujol or hexachlorobutadiene) had maxima at 3305, 3060, 2920, 1679 (s), 1663 (s), 1640 (s), 1536 (s), 1469, 1437, 1420, 1407, 1385, 1375, 1370, 1336, 1289, 1255, 1244, 1160, and 1020 cm.$^{-1}$.

(*b*) When 6N-hydrogen bromide in acetic acid (1·75 c.c.) was added to a suspension of benzyloxycarbonylglycyl-L-leucylglycine *p*-nitrophenyl thiolester [5] (0·900 g.) in acetic acid (6·5 c.c.), a clear solution was formed at once. After this had been kept at room temperature during 40 min., it was worked up and the material still soluble in ethyl acetate was treated again with hydrogen bromide, as in the foregoing experiments. The combined aqueous solutions were added during 4 hr. to a stirred suspension of magnesium carbonate (1·4 g.) in water (400 c.c.). The cyclic hexapeptide (0·046 g., 11·5%) was isolated as in (*a*) above [Found: C, 53·3; H, 7·1; N, 18·6%; *M* (ebullioscopic [12]), 424], $\nu_{max.}$ 3305, 3060, 2920, 1679 (s), 1662 (s), 1640 (s), 1536 (s), 1465, 1436, 1420, 1407, 1385, 1370, 1335, 1288, 1256, 1245, 1164, 1020 cm.$^{-1}$.

In an earlier experiment on half the above scale, cyclisation was carried out by adding the whole hydrobromide solution to a suspension of magnesium oxide (1 g.) in 4 l. of water. The cyclic hexapeptide (16%) was isolated, without use of ion-exchange columns, by partition between butan-1-ol (100 c.c.), ethyl acetate (100 c.c.), and 2N-sulphuric acid (50 c.c.) followed, after washing of the organic layer with saturated sodium hydrogen carbonate solution (50 c.c.) and water (50 c.c.) and back-extractions, by countercurrent distribution (19 transfers) in the system ethyl acetate–methanol–water (10 : 1 : 9 volumes); the material in tubes 0—7 was distributed (14 transfers) in the system ethyl acetate–butan-1-ol–water (10 : 1 : 9 volumes), and the colourless crystalline product (*K* 0·65) was recovered from tubes 3—9 before being recrystallised from methanol–ether.

Measurement of Dielectric Increments.—The capacitance of a cell was measured at 30·5° with a Twin-T bridge (General Radio type 821-A), a communications receiver, and a signal generator maintained at 28 Mc. by frequent reference to a separate crystal-controlled oscillator. Like this circuit, the cell design was taken from the literature [23] apart from the addition of a capillary tube at the bottom; through this tube the cell could be filled, emptied, washed, and dried and it was not dismantled during a series of measurements. The cell was calibrated with solutions of glycine, 22·33 being used as its dielectric increment,[24] by plotting the difference between the readings on the dial of the precision condenser when the bridge was balanced with the solution and with water against the concentration of glycine. A straight line was obtained and this direct comparison was preferred to the evaluation of the *actual* capacitance in each case by allowance for conductance. Measurements were made with three concentrations of the peptides between 0·009M and 0·025M. The dielectric increment of tetraglycine was found to be 162·3 (±1·3), while 165·8 [23] and 159·2 [25] are recorded for 25°. The value for the L-L-pentapeptide was 186·0 (±0·9) and for the L-D-isomer 168·9 (±1·3).

The free peptides were prepared by hydrogenolysis of their benzyloxycarbonyl derivatives in 50% aqueous methanol, or in methanol containing a few drops of acetic acid, with charcoal bearing 10% of palladium. The peptides left on evaporation contained traces of salt, which gave their solutions too much conductance for balance of the Twin-T bridge, and these were removed by electrodialysis at 100 v. through a Cellophane sack. *Glycyl-L-leucylglycyl-L-leucylglycine* (Found: C, 49·3; H, 8·2; N, 15·4. $C_{18}H_{33}O_6N_5,1{\cdot}5H_2O$ requires C, 48·9; H, 8·2; N, 15·8%) and *glycyl-L-leucylglycyl-D-leucylglycine* (Found: C, 48·9; H, 8·2%) were obtained as sesquihydrates by precipitation with ethanol from aqueous solution.

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[23] Conner, Clarke, and Smyth, *J. Amer. Chem. Soc.*, 1942, **64**, 1379.
[24] Linquist and Schmidt, *Compt. rend. Trav. Lab. Carlsberg*, 1938, **22**, 307.
[25] Wyman and McMeekin, *J. Amer. Chem. Soc.*, 1933, **58**, 608.

836. *Structural Chemistry of the Alkoxides. Part XI.*[1] *Branched-chain Alkoxides of Iron*(III).

By D. C. Bradley, R. K. Multani, and W. Wardlaw.

Ferric alkoxides $Fe(OR)_3$, where R = Pr^i, Bu^s, Bu^t, Pr^iMeCH, Pr^nMeCH, Et_2CH, $EtMe_2C$, Et_2MeC, Pr^nMe_2C, or Et_3C, have been prepared. Determinations of molecular weights and volatilities revealed the effect of chain branching of the alkyl group on the physicochemical properties. These results are compared with those on the corresponding aluminium derivatives and some interesting differences in behaviour are apparent.

Recently we reported[1] the preparation and properties of some primary alkoxides of iron(III). The normal alkoxides $Fe(OC_nH_{2n+1})_3$, where n = 1, 2, 3, 4, or 5, were all trimers in boiling benzene (cf. aluminium derivatives, which are tetramers[2]) whereas the *neo*-pentyloxide was dimeric; hence it was clear that a systematic investigation of the effect of chain branching would be interesting. The comparison between the alkoxides of aluminium and ferric iron is particularly so in connection with our stereochemical theory for the alkoxides because of the similarity in atomic size of these elements and their analogous stereochemistry. This should lead to a similarity in degrees of polymerisation for aluminium and ferric alkoxides with the same alkoxide groups.

Accordingly, branched-chain alkoxides of iron have been prepared either by alcohol interchange or by the reaction involving ferric chloride, the alcohol, and ammonia in benzene.

Table 1.

	M = Al[2]			M = Fe		
R in $M(OR)_3$	B. p./5·0 mm.	*M*	*n*	B. p./0·1 mm.	*M*	*n*
Bu^n	270°	962	3·9	171°	873	2·9
Bu^i	—	—	—	173	884·5	3·0
Bu^s	172	580	2·4	159	522	1·9
Bu^t	—	480	1·95	136	412	1·5

Ferric iso*Propoxide.*—This was a dark-brown crystalline solid which sublimed without decomposition at 149°/0·1 mm. and was dimeric in boiling benzene. By contrast aluminium *iso*propoxide, which is trimeric,[2] is considerably more volatile, b. p. 124°/5 mm.[2]

Isomeric Butoxides of Iron.—These were all obtained by alcohol interchange by use of ferric ethoxide[1] and the appropriate alcohol. All except the *tert.*-butoxide were also prepared by the ammonia method with ferric chloride. This method gave a hydrolysed product for *tert.*-butyl alcohol, but a pure product resulted when ferric chloride was replaced by the less reactive pyridinium salt $(C_5H_6N)_3Fe_2Cl_9$. Molecular weights (ebullioscopic in benzene), degree of polymerisation (n), and volatilities are shown in Table 1 which also contains results for some corresponding aluminium alkoxides.[2] The butoxides of iron and aluminium both exhibit the expected decrease in degree of polymerisation and increase in volatility with increased branching of the butyl group. However, the ferric butoxides are uniformly lower in degree of polymerisation than the corresponding aluminium compounds. In fact the *tert.*-butoxide of iron must contain a considerable proportion of monomer. Furthermore, although Mehrotra[2] has demonstrated that aluminium *tert.*-butoxide cannot be obtained by alcohol interchange owing to the formation of the stable mixed alkoxide $Al(OR)(OBu^t)_2$, we find that ferric *tert.*-butoxide can be obtained directly by alcohol interchange.

Isomeric Pentyloxides of Iron.—All these were prepared by alcohol interchange with ferric ethoxide. The derivatives of *n*-, *iso*-, or *sec.*-butylcarbinol (*n*-pentanol, *iso*pentanol,

[1] Part X, Bradley, Multani, and Wardlaw, *J.*, 1958, 126.
[2] Mehrotra, *J. Indian Chem. Soc.*, 1953, **30**, 585; 1954, **31**, 85.

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or 2-methylbutanol) were also prepared from ferric chloride by the ammonia method. The *tert.*-amyloxide was also obtained by the ammonia method involving the pyridinium ferrichloride. The volatilities, molecular weights (ebullioscopic in benzene), and degrees of polymerisation are in Table 2.

These results show clearly how chain branching affects the degree of polymerisation and consequently the volatility of the isomeric pentyloxides. That this is essentially a steric effect due to the shielding exerted by the alkoxide groups is shown by the behaviour of the *neo*pentyloxide group which forms a derivative similar in physicochemical properties to the secondary pentyloxides. A comparison of the properties of aluminium and ferric pentyloxides is interesting. Although in the primary pentyloxides (and *neo*pentyloxide) the aluminium derivatives have higher degrees of polymerisation, yet in the secondary pentyloxides (and *neo*pentyloxide) the aluminium and iron alkoxides have the same degrees of polymerisation.

TABLE 2.

	M = Al [2]			M = Fe		
R in $M(OR)_3$	B. p./mm.	*M*	*n*	B. p./0·1 mm.	*M*	*n*
Bu^nCH_2	255°/1·0	1152	4·0	178°	952	3·0
Bu^iCH_2	195/0·1	1160	4·0	dec. 200	941	3·0
Bu^nCH_2	~200/0·6	1194	4·1	178	951	3·0
Bu^iCH_2	180/0·8	598	2·1	159	634	2·0
Et_2CH	165/1·0	601	2·1	163	634	2·0
Pr^nMeCH	162/0·5	596	2·1	165	602	1·9
Pr^iMeCH	162/0·6	572	2·0	162	604	1·9
$EtMe_2C$	—	—	—	131	476	1·5

Again, although Mehrotra [2] found that aluminium *tert.*-amyloxide could not be obtained by alcohol interchange we were able to prepare the ferric derivative by this method and it is clear that the latter has an important proportion of monomer. This led us to explore the possibilities of making a completely monomeric ferric alkoxide by using even larger branched alkyl groups. The ferric derivatives of 3-methylpentan-3-ol, 2-methylpentan-2-ol, and 3-ethylpentan-3-ol were obtained by alcohol interchange on the ethoxide and all were monomeric in boiling benzene. They were dark red liquids boiling at 137°/0·1, 135°/0·1, and 132°/0·1 mm. respectively. To summarise all the available data on aluminium and ferric alkoxides, it seems that in general the aluminium derivative has a higher degree of polymerisation than the corresponding ferric compound. It is tempting to explain this in terms of stronger intermolecular bonding in the aluminium alkoxides but this would cause them to be less volatile than ferric alkoxides, which is contrary to the facts. However, it must be remembered that Mehrotra found " ageing " effects with the aluminium alkoxides and this might vitiate a comparison of their degrees of polymerisation with those of ferric compounds.

EXPERIMENTAL

Apparatus and techniques were similar to those described previously.[1]

Tripyridiniumiron Enneachloride.—A solution of ferric chloride (5·6 g.) in ethyl alcohol (150 c.c.) was saturated with dry hydrogen chloride. Pyridine (7·8 g.) was then added and the solution again saturated with hydrogen chloride. After removal of alcoholic hydrogen chloride under reduced pressure the residue was heated at 120°/0·5 mm. until no more pyridinium chloride was evolved. A yellow-green *solid* remained on cooling [Found: Fe, 16·3; Cl, 46·8. $(C_5H_6N)_3Fe_2Cl_9$ requires Fe, 16·6; Cl 47·5%].

Ferric iso*Propoxide.*—*iso*Propyl alcohol (58·6 g.) was added dropwise to the frozen (*ca.* − 10°) mixture of ferric chloride (11 g.) and benzene (200 g.) with continued cooling. Ammonia was passed in slowly in excess and after storage for 12 hr. at room temperature the volatile components were evaporated off under reduced pressure. The residue of ammonium chloride and ferric *iso*propoxide was extracted with benzene (*ca.* 150 g.) and the *ferric* iso*propoxide* obtained as a dark brown crystalline solid (3·5 g.) after evaporation of the benzene [Found: Fe, 24·2; Pr^iO, 75·6. $Fe(OPr^i)_3$ requires Fe, 24·0; Pr^iO, 76·0%].

Ferric tert.-*Butoxide*.—Pyridiniumferric chloride (15 g.) was suspended in a cold (*ca.* 5°) mixture of benzene (200 g.) and *tert.*-butyl alcohol (50 g.). Ammonia was passed in and the *ferric* tert.-*butoxide* isolated as in the previous experiment. A brown solid (3·4 g.) was obtained. [Found: Fe, 20·2. $Fe(OBu^t)_3$ requires Fe, 20·3%].

Preparation of Other Ferric Alkoxides.—Ferric *alkoxides* were prepared either by the two foregoing methods or by alcohol interchange on ferric ethoxide.[1] The essential data are in Table 3.

TABLE 3.

R in $Fe(OR)_3$	Taken *	C_6H_6 (g.)	ROH (g.)	$Fe(OR)_3$ (g.)	Fe (%) Found	Calc.
Bu^n	5·0 [a]	150	29	2·5	20·1	20·3
Pr^iMeCH	5·0 [a]	80	40·5	8·0	17·4	17·6
Pr^nMeCH	5·0 [a]	80	50	8·1	17·3	17·6
$EtMe_2C$	20·8 [b]	200	50	4·8	17·4	17·6
,,	3·0 [c]	100	15·5	4·8	17·5	17·6
Et_2MeC	3·0 [c]	100	12·0	5·6	15·5	15·6
Et_3C	2·8 [c]	100	10·0	4·3	13·6	13·7

* Weight (g.) of (*a*) Fe_2Cl_6, (*b*) $(C_5H_6N)_3Fe_2Cl_9$, or (*c*) $Fe(OEt)_3$.

TABLE 4.

R in $Fe(OR)_3$	*m* (g.)	C_6H_6 (g.)	$\Delta T/m$ (°/g.)	*M* Found	Calc.
Pr^i	0·0213—0·1986	18·0	0·351	466 [a]	232·8
Bu^n	0·0423—0·2226	18·0	0·314	522 [b]	278·4
Et_2CH	0·0481—0·2986	16·3	0·284	634	316·8
Pr^nMeCH	0·0438—0·2831	17·0	0·273	602	316·8
Pr^iMeCH	0·0724—0·3623	18·4	0·252	604	316·8
Me_2C	0·0413—0·2788	16·9	0·422	412	278·4
$EtMe_2C$	0·0410—0·1866	18·3	0·338	476	316·8
Et_2MeC	0·0362—0·1941	16·0	0·513	359	358·8
Pr^nMe_2C	0·0521—0·3621	17·5	0·468	360	358·8
Et_3C	0·0411—0·1882	18·25	0·402	402 [a]	400·8

Found by " internal calibration " method [1] (*a*) $M = 462$, (*b*) $M = 529$, (*c*) $M = 399$.

Molecular Weights.—Measurements were carried out with techniques previously described [3] (Table 4).

One of us (R. K. M.) thanks the Hans Raj College (Delhi University) for study leave.

BIRKBECK COLLEGE, MALET STREET, LONDON, W.C.1. [*Received, July 25th*, 1958.]

[3] Bradley, Gaze, and Wardlaw, *J.*, 1955, 3977; Bradley, Wardlaw, and Whitley, *J.*, 1956, 5.

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837. *Infrared Absorption of Heteroaromatic and Benzenoid Six-membered, Monocyclic Nuclei. Part IV.*[1] *Monosubstituted Benzenes.*

By A. R. KATRITZKY and (MRS.) J. M. LAGOWSKI.

The infrared absorption due to the phenyl group in eighty-five compounds is recorded. The variations of the positions and the intensities of the characteristic bands with the nature of the substituent are discussed.

IN monosubstituted pyridines,[1,2,3] pyridine 1-oxides,[4,5,6] pyridine–boron trichlorides,[7] and furans [8] all the bands, with few exceptions, are characteristic of either the nucleus or the substituent. Further, the position and intensity of each nuclear band are either

[1] Part III, Katritzky, Hands, and R. A. Jones, *J.*, 1958, 3165. Parts I—III were published under the series title " Infrared studies of heterocyclic compounds."
[2] Katritzky and Gardner, *J.*, 1958, 2198.
[3] Katritzky and Hands, *J.*, 1958, 2202.
[4] Katritzky and Gardner, *J.*, 1958, 2192.
[5] Katritzky and Hands, *J.*, 1958, 2195.
[6] Katritzky, Beard, and Coates, unpublished work.
[7] Katritzky, unpublished work.
[8] Katritzky and Lagowski, *J.*, in the press.

reasonably constant or vary regularly with the type of substituent to which the nucleus is attached. We examined monosubstituted benzenes (i) to check the bands due to the phenyl groups in the pyridines and pyridine 1-oxides, (ii) to investigate the variations in the positions and intensities of the benzenoid nuclear bands with the nature of the substituent, and (iii) to compare the bands due to substituents in these compounds with those due to the same substituents in the heterocyclic compounds. We needed the information under (ii) to explain the intensity variation of nuclear bands in the heterocyclic compounds in terms of the variation of the dipole-moment during the vibration (see following paper).

The spectra were measured in chloroform, and apparent extinction coefficients were recorded.[9] Solvent absorption obscured the out-of-plane C–H deformation modes [10a, 11a] below 800 cm.$^{-1}$; the concentration used was not sufficient to distinguish the combination frequencies [10b, 11b] between 2000 and 1650 cm.$^{-1}$, and the sodium chloride prism gave poor resolution of the C–H stretching modes [10c, 11c] in the 3000 cm.$^{-1}$ region. Thus, this work is concerned with modes of predominantly C–C stretching at 1600—1400 cm.$^{-1}$ and CH in-plane deformation character at 1200—1000 cm.$^{-1}$; six bands were characteristic (Table 1), and four others appeared only in certain types of compound (Table 2 and text).

Randle and Whiffen [12] treated statistically the spectra of many monosubstituted benzenes and listed arithmetical means and standard deviations for twenty characteristic bands. They obtained data from many sources measured under varying conditions and were unable to give precise intensities or to correlate the intensity or position of a band with the type of substituent. Of the twenty bands, ten correspond to those given in Tables 1 and 2 (cf. last row). Three bands below 800 cm.$^{-1}$ and one at *ca.* 1240 cm.$^{-1}$ would be obscured by solvent in our work; the remaining six, near 837(w), 962(w), 982(vw), 1324(w), 1387(w), and 1663(w) cm.$^{-1}$, are evidently too weak to be distinguished under our conditions. Early work has been summarised.[13] Bellamy [11d] indicates that monosubstituted benzenes absorb at 1600 $\pm$ 5 cm.$^{-1}$, near 1580 and 1500 cm.$^{-1}$, and in each of the regions 1175—1125 (weak), 1110—1070, and 1070—1000 cm.$^{-1}$. The only indication of the position depending on the substituent was that bromo-, chloro-, and mercaptobenzene absorb near 1595 cm.$^{-1}$ but nitrobenzene near 1605 cm.$^{-1}$. The intensities were stated to be " notorious for very wide fluctuations "; the 1580 cm.$^{-1}$ band was very weak except when conjugated with a nitro-, carbonyl, or unsaturated group. Such conjugation was stated to enhance markedly, in most cases, the intensity of the 1600 and 1500 cm.$^{-1}$ bands also, but occasionally the 1500 cm.$^{-1}$ band became less intense. Jones and Sandorfy [10b] state that the simpler aromatic compounds absorb between 1610—1590 and 1500—1480 cm.$^{-1}$; their intensity data compare reasonably well with ours. Twenty monosubstituted benzenes showed [14] four characteristic bands in the 1600—1400 cm.$^{-1}$ region; the frequencies of the eleven compounds which we too have measured agree well; our peaks are [0·7 $\pm$ 2·4] cm.$^{-1}$ higher. Four bands found by McMurry and Thornton [15] at 1200—800 cm.$^{-1}$ are discussed below.

Band Near 1600 *cm.*$^{-1}$ (*Table* 1, *col.* 1).—A band occurs at 1611—1599 [1604 $\pm$ 3] ‡ cm.$^{-1}$ for all the compounds except that the frequency is lowered to 1588—1581 cm.$^{-1}$ if a heavy atom (Cl, Br, or SH; Nos. 67—69) is attached directly to the nucleus (similar behaviour is found in other series [1–6]); in the only other exception, No. 49, the band is due mainly to

[9] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[10] Jones and Sandorfy in Weissberger, " Technique of Organic Chemistry, Vol. IX. Chemical Applications of Spectroscopy," Interscience Publ. Inc., New York, 1956: (*a*) p. 388, (*b*) p. 397, (*c*) p. 392, (*d*) p. 343.
[11] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1956: (*a*) p. 64, (*b*) p. 57, (*c*) p. 55, (*d*) pp. 59—63.
[12] Randle and Whiffen, Report on Conference on Molecular Spectroscopy, 1954, Institute of Petroleum, Paper No. 12.
[13] Depaigne-Delay and Lecomte, *J. Phys. Radium*, 1946, **7**, 38.
[14] Josien and Lebas, *Bull. Soc. chim. France*, 1956, 53, 57.
[15] McMurry and Thornton, *Analyt. Chem.*, 1952, **24**, 318.

substituent absorption. The intensity is high (125—290) [(200 ± 55)] ‡ for compounds with strong electron-donating substituents (Nos. 1—15), intermediate (25—45) for the sulphonamido-compounds (Nos. 16—17), and low (5—35) [(20 ± 7)] for compounds with a saturated carbon atom or a carbon–carbon multiple bond attached directly to the nucleus (Nos. 18—66). Higher intensities are shown again for halogeno- and thio-compounds (Nos. 67—69) (40—60) and for compounds carrying other electron-withdrawing substituents (Nos. 71—85) (30—80) [(50 ± 20)] except cyanobenzene (No. 70).

Band Near 1580 *cm.*$^{-1}$ (*Table* 1, *col.* 2).—Compounds with a saturated carbon atom adjacent to the ring (Nos. 18—46) show only a weak shoulder or do not absorb in this region, but an olefinic group next to the ring (Nos. 47—55) consistently causes absorption at 1581—1579 cm.$^{-1}$ (10—30). Shoulders sometimes occur for the ethynyl- and aryl-substituted compounds (Nos. 56—66), but the region is obscured too often by substituent absorption to permit generalisation. The halogeno-compounds show weak shoulders at *ca.* 1562 cm.$^{-1}$. The band is stronger for compounds with electron-withdrawing substituents (Nos. 71—85), 1588—1580 cm.$^{-1}$ (20—70) [1585 ± 3 cm.$^{-1}$ (35 ± 10)], except for the cyano-compound (No. 70). Compounds with electron-donating substituents show a strong band at *ca.* 1600 cm.$^{-1}$ which often masks this region; however, the ethers (Nos. 6—8) exhibit a well resolved band at *ca.* 1590 cm.$^{-1}$ (*ca.* 85). Thus, for benzyloxybenzene (No. 8) the band is due to the phenolic ring. The absorption bands shown by benzanilide and *N*-methylbenzanilide (Nos. 12, 14) are associated with the benzoyl rings, because acetanilide and *N*-methylacetanilide (Nos. 13, 15) do not show resolved bands.

Band Near 1500 *cm.*$^{-1}$ (*Table* 1, *col.* 3).—Nearly all the compounds show a band at 1511—1477 cm.$^{-1}$. Electron-donating groups (Nos. 1—17) cause absorption at 1511—1493 [1498 ± 5] cm.$^{-1}$, which is somewhat higher than for compounds with a saturated, olefinic, or acetylenic carbon atom adjacent to the ring (Nos. 18—59) absorbing at 1500—1490 [1494 ± 2] cm.$^{-1}$ (except Nos. 23, 31, and 42 where most of the absorption arises from the substituent). An aromatic ring directly attached to the nucleus (Nos. 60—66) lowers the frequency to 1483—1470 cm.$^{-1}$ and a heavy atom (Nos. 67—69) to 1483—1477 cm.$^{-1}$. Intensities are high (100—220) [(145 ± 40)] for compounds with electron-donating (including sulphonamido-, halogeno-, and thio-)substituents (Nos. 1—17, 66—69), intermediate (15—65) [(40 ± 10)] for saturated or olefinic substituents (Nos. 18—55), but variable (55—230) for the ethynyl-substituents (Nos. 56—59). The band is weak or absent for compounds carrying electron-withdrawing substituents (Nos. 71—86) except cyanobenzene.

Band Near 1450 *cm.*$^{-1}$ (*Table* 1, *col.* 4).—Strong absorption (210—340) is shown by non-*N*-substituted-carbonamido-compounds (Nos. 10, 13, 15) at 1447—1440 cm.$^{-1}$; other electron-donating substituents (Nos. 1—9, 16—7) cause absorption at 1465—1445 cm.$^{-1}$ (25—45) [1456 ± 7 cm.$^{-1}$ (30 ± 10)]. Nuclei with a saturated substituent (Nos. 18—46) absorb at 1458—1450 [1454 ± 2] cm.$^{-1}$; the intensities are intermediate (25—65) [(45 ± 15)] except for the methyl esters Nos. 26 and 52 where the band is strongly overlapped by methoxyl absorption and, inexplicably, the 2-pyridylthiomethyl compound, No. 38. Compounds with an olefinic carbon atom adjacent to the ring (Nos. 47—55) absorb at 1452—1450 cm.$^{-1}$ (30—80) [1451 ± 1 cm.$^{-1}$ (50 ± 20)] with an acetylenic carbon atom (Nos. 56—59) at 1445—1443 cm.$^{-1}$ (20—25), with an aromatic ring (Nos. 61—66) at 1455—1451 cm.$^{-1}$ (except in diphenyl where the band is split) (10—110), and with a heavy atom (Nos. 66—69) at 1447—1446 cm.$^{-1}$ (30—60). Electron-accepting substituents (Nos. 70—85) cause absorption at 1455—1448 cm.$^{-1}$ (25—75, except for No. 79 where the band is overlapped by substituent absorption), but the nitro-compound shows only a weak

‡ Throughout this paper values in parentheses are apparent molecular extinction coefficients. Values in brackets are arithmetical means and standard deviations of the positions and intensities, calculated by omitting those compounds where the band is present as a shoulder, and, in the case of ε_A, those in which it is superimposed on another band or the result of absorption by more than one benzene ring in different environments. When the molecule contains two benzene rings in the same environment, ε_A values are halved in the statistical treatment.

TABLE 1.

No.	Substituent	A_1 νCC cm.$^{-1}$	ε_A	B_1 νCC cm.$^{-1}$	ε_A	A_1 νCC cm.$^{-1}$	ε_A	B_1 νCC cm.$^{-1}$	ε_A	B_1 βCH cm.$^{-1}$	ε_A	A_1 βCH cm.$^{-1}$	ε_A
1	NMe_2	1605	250	1577 *	40	1500	140		(—)		(—)	1030	35
2	NHMe [a]	1610	290		—	1511	220	1453	30	1072	25	1022	5
3	NH·Ph [a]	1598	*480*		(—)	1514 *	*340*	1464	*55*	1081	*20*	1026	*40*
						1498	*380*			1073	*20*		
4	NH·4Py	1610 *	130		(—)	1499 *	150	1445	45	1074	15	1029	15
5	NH_2	1605	125		—	1495	110	1465	25		—	1026	10
6	OMe	1601	140	1591 *	85	1494	135	1453	40	1077	45	1018 *	35
7	OEt	1602	135	1589	80	1494	120	1458	25	1076	40		(—)
8	OCH_2·Ph	1602	*150*	1590	*90*	1493	*170*	1453	*60*	1075	*35*	1027	*85*
9	OH [a]	1603	170		—	1503	170		(—)	1069	40	1023	15
10	NH·CO_2Et [a]	1601	200		(—)	1505 *	145	1447	340		(—)	1024 †	95
11	NMe·COMe	1601	240		(—)	1497	190		(—)	1073	20	1023	25
12	NMe·COPh	1600	*260*	1583	*140*	1496	*250*	1460 *	60	1075	*45*	1031	*45*
								1448	80				
13	NH·COMe [a]	1604	210		—	1502	220	1442	270	1077	15	1030	30
						1488 *	70						
14	NH·COPh [d]	1604	*225*	1581	85	($CHCl_3$)		($CHCl_3$)		1072	*80*	1026	*55*
15	NH·$COCH_2$·4Py	1602 †	260		—	1500 *	160	1440	210	1078	10		—
16	NMe·SO_2Me	1603	25		—	1494	100	1455	25	1075 *	55	1025	25
17	NH·SO_2Me	1605	45		—	1495	100	1460 *	20	1077	20	1029	25
18	Me	1603	20		—	1496	45	1455	25	1081	20	1028	20
19	Et	1609	15		—	1495	35	1454	50		—	1028	20
20	CH_2·CH_2·Ph	1605	*40*		—	1494	*90*	1454	*80*	1066	*20*	1028	*35*
21	CH_2·CH_2·4Py		(—)		(—)	1496	50	1455	45	1070 †	20	1030	15
22	CH_2·CH_2·2Py		(—)		(—)	1495	45	1454	40	1071	15	1030	10
23	CH_2·CH_2·4PyO	1606	15		—	1487 †	280	1451 †	90	1072	15	1030 *	15
24	CH_2·CH_2·2PyO	1606	20		—	1491 †	105	1453 *	65	1071	15	1030	10
25	CH_2·CH_2·NH·CS·CH_2·4Py		(—)		(—)	1480 *	45	1453 *	65	1079 *	25	1028	15
26	CH_2·CH_2·CO_2Me	1609	15		—	1497	40	1455	80	1079	35	1028 †	35
27	CH_2·CH_2·CO_2Et	1609	15		—	1495	40	1454	65	1078	55		(—)
28	CH_2·Ph	1601	*30*	1587 *	*15*	1491	*75*	1450	*50*	1075	*30*	1029	*35*
29	CH_2·4Py		(—)		(—)	1493	40	1452	25	1069 †	30	1029	15
30	CH_2·2Py		(—)		(—)	1493	40	1451	30	1072	10	1029	15
31	CH_2·4PyO	1603	20		—	1485 †	280	1450 †	80	1071	10	1030	30
32	CH_2·2PyO	1607	30		—	1490 †	105	1454 *	40	1074	15	1030	10
33	CH_2·CO·NH·CH_2·CH_2·4Py		(—)		(—)	1495 *	155	1454	60		(—)	1028	20
34	CH_2·CO_2Me	1609	15	1590 *	10	1497	50	1457	55	1075	15	1030 *	20
35	CH_2·CO_2Et	1607	15	1587 *	10	1497	40	1454	45	1074	25	1028 †	130
36	CH_2·NH·$COCH_2$·4Py		(—)		(—)	1500 *	210	1452	55	1078	20	1027	15
37	CH_2·S·4Py	1608 *	20		(—)	1494	50	1453	50		(—)	1028	20
38	CH_2·S·2Py	1609 *	20		(—)	1495	60	1456	195	1069	25	1028	20
39	CH_2·S·4PyO	1605	20		—	1496	50	1458 *	170	1070	25		(—)
40	CH_2·S·2PyO	1608 *	10		(—)	1496	55	1454	65	1070	20	1028	20
41	CH_2·O·2Py		(—)		(—)	1495	35	1454	65		—	1026 *	50
42	CH_2·O·4PyO		(—)		(—)	1485 †	360	1456 †	105	1079	10	1026 *	110
43	CH_2·OH	1600	5		—	1492	15	1454	40	1075 *	15	1035 *	50
44	CHPh·OH [a]	1604	*20*		(—)	1497	*80*	1456	*90*	1081	*15*	1030 *	*70*
45	CH(4Py)OH		(—)		(—)	1492	40	1453	45	1077	20	1025	70
46	CH(2Py)OH		(—)		(—)	1494	40	1457	60	1080	35	1027	90
47	CH:CH·Ph	1602	*50*	1582	*15*	1495	*65*	1451	*60*	1070	*30*	1028	*20*
48	CH:CH·4Py		(—)		(—)	1495	25	1450	30	1073	10	1027	5
49	CH:CH·2Py	1592 †	180		(—)	1494	65	1451	45	1073	10	1029	5
50	CH:CH·4PyO [a]	1600	15	1580	10	1493 *	150	1452 †	75	1073	15	1032 †	110
51	CH:CH·2PyO	1610 †	50	1579	15	1493 *	75	1450	60	1071	15	1027	15
52	CH:CH·CO_2Me	1610 *	20	1581	30	1493	35	1451	115	1070	25	1026 *	30
53	CH:CH·CO_2Et		(—)	1580	20	1495	30	1450	80	1069	40	1028 *	95
54	CH:C(4Py)(COMorph [a])		(—)		(—)	1493	55		(—)	1070 †	65	1027	20
55	CH:CH·4Py·BCl_3 [d]		(—)	1580 *	50	(1493	30)	($CHCl_3$)			(—)	1026 *	10
56	C:C·Ph	1608	*55*	1573	*5*	1500	*125*	1445	*55*	1070	*30*	1026	*30*
57	C:C·4Py	1608 *	165		(—)	1500	55	1445	25	1062 *	10	1025	15
58	C:C·2Py	1601	35		(—)	1490	105	1443	20	1065	10	1025	10
59	C:C·4PyO	1600	30		—	1495	235	1445 †	55	1065	15	1032 †	130
60	Ph	1600	*40*	1568	*15*	1483	*135*	1460 *	*15*	1073	*30*	1042	*15*
								1431	*40*				
61	4Py	1610 *	80		(—)	1480	55	1446 *	10	1076 *	15	1040	10
62	3Py		(—)		(—)		(—)	1450	55	1072	10	1023 †	30

TABLE 1. (*Continued.*)

No.	Substituent	A_1 νCC cm.$^{-1}$	ε_A	B_1 νCC cm.$^{-1}$	ε_A	A_1 νCC cm.$^{-1}$	ε_A	B_1 νCC cm.$^{-1}$	ε_A	B_1 βCH cm.$^{-1}$	ε_A	A_1 βCH cm.$^{-1}$	ε_A
63	2Py	1607 *	20	(—)		1470 †	130	1451	110	1072	15	1019	20
64	4PyO [b]	1605	25	1585 *	10	1500 *	25	(—)		1076	10	(—)	
65	3PyO	(—)		1582 *	25	1472 †	120	1455	65	1078	10	1028 *	10
66	2PyO	1611	10	1580	10	1478 †	130	1451	35	1075	10	1016	65
67	SH [c]	1588	45	(—)		1483	110	1446	55	1091 1068	30 10	1023	45
68	Cl	1587	40	1562 *	10	1479	110	1447	30	1084 1063 *	80 20	1023	65
69	Br [c]	1581	60	1563 *	10	1477	145	1446	60	1067	120	1018	95
70	·C≡N [c]	1604	15	1585 *	5	1495	45	1452	40	1068	10	1025	20
71	CO·NH·4Py [d]	(—)		(—)		($CHCl_3$)		($CHCl_3$)		1072 †	45	1027	40
72	CO·NH·3Py	1603 *	90	(—)		(—)		1448	25	1073	25	1026 †	45
73	CO·NH·2Py	(—)		(—)		(—)		1447 *	95	1072	30	1027	35
74	CO·NH·2PyO	(—)		(—)		(—)		1449 *	80	1069	50	1027	30
75	CO·NMe·3Py	1613 *	60	(—)		(—)		1450 *	75	1075	15	1023 †	80
76	CO·NMe·2Py	(—)		(—)		1472 †	260	(—)		1075	20	1029 *	15
77	CO·NMe·4PyO	1610 *	70	1582	45	1487 †	510	1451 †	100	1074	20	1030	80
78	CO·NMe·2PyO	(—)		1580	40	(—)		1450 *	100	1075	30	1028	20
79	CO_2Me	1605	40	1582	20	1490	10	1453	95	1071	60	1026	60
80	CO_2Et	1606	30	1588	25	1490 *	5	1451	75	1070	90	1028 †	140
81	$CO_2CMe(CN)$·4Py	(—)		(—)		1490	15	1451	75	(—)		(—)	
82	CHO	1601	80	1588	70	—		1455	25	1070	10	1021	10
83	COMe	1601	55	1585	30	—		1448	55	1075	20	1022	30
84	CO·CH_2·4Py	(—)		1588	50	1499	10	1452	75	1071 †	30	1020 *	20
85	NO_2	1621 * 1609	25 30	1590 *	20	1478	30	1458 *	15	1068	25	1021	30
	(*f*)	[1606 ± 7] m		[1588 ± 9] w		[1499 ± 7] vs		[1451 ± 12] s		[1072 ± 7] m		[1029 ± 5] s	

Assignments of symmetry and type of vibration (from ref. 12) are given at tops of columns.

* Shoulder, † absorption considered to be the superimposition of two peaks, — absence of absorption, (—) band masked by stronger absorption, ($CHCl_3$) band masked by solvent, Ph phenyl, Py substituted pyridine(4Py = 4-pyridyl, etc.), PyO substituted pyridine 1-oxide.

ε_A *in italics* denotes absorption by two benzene rings.

[a] These substances were measured at Cambridge, the others at Oxford. [b] Extra band at 1301 (20). Extra band at 1145 (85). [d] Measured at 0·02M in 1 mm. cell because of poor solubility. [e] Morpholide. [f] Arithmetical means and standard deviations reported by Randle and Whiffen.[12]

TABLE 2.

No.	Subst.	A_1 βCH cm.$^{-1}$	ε_A	B_1 βCH cm.$^{-1}$	ε_A	A_1 ring cm.$^{-1}$	ε_A	B_2 γCH cm.$^{-1}$	ε_A
1	NMe_2	(—)		1160	45	991	50	860	10
2	NHMe	1181	65	(—)		990	20	868	25
3	NH·Ph	1175	*55*	1155	*20*	995	*15*	871	*30*
4	NH·4Py	1170 *	15	—		(—)		885	30
5	NH_2	1173	25	1150	10	994	10	878	25
6	OMe	1177 * 1171	45 60	1151	20	992	15	882	20
7	OEt	1170	60	1151	25	995 *	10	883	20
8	OCH_2·Ph	1170	*70*	1151	*20*	992	*25*	913 882	10 20
9	OH	1169 *	100	(—)		998	15	882	20
10	NH·CO_2Et	1178	70	1158	30	998 *	10	894	15
11	NMe·COMe	(—)		(—)		—		—	
12	NMe·COPh	1174	*25*	—		997	*20*	(—)	
13	NH·COMe	1176	15	—		1002	25	898	15
14	NH·COPh	($CHCl_3$)		($CHCl_3$)		—		883 899	20 15
	Randle and Whiffen [12]	[1177 ± 6] m		[1156 ± 5] m		[1001 ± 4] Var		[908 ± 10] mw	

shoulder at 1458 cm.$^{-1}$. This band is often overlapped by substituent C–H deformations, sometimes making interpretation of the intensities difficult.

Bands at 1200—1100 *cm.*$^{-1}$ (*Table* 2, *cols.* 1 *and* 2).—Randle and Whiffen [12] found two bands in practically all the spectra examined. We find that most of the compounds with

electron-donating substituents absorb at 1181—1170 cm.$^{-1}$ (15—100) and 1160—1150 cm.$^{-1}$ (10—45). Of the remaining seventy-one compounds, forty-three absorb ($\varepsilon_A > 10$) in this region; however, all bands could be assigned to substituents. In agreement, McMurry and Thornton [15] found these bands in hydrocarbons at 1184—1176 and 1160—1152 cm.$^{-1}$ with average ε_A of (5) and (4),¶ respectively.

Band Near 1070 *cm.*$^{-1}$ (*Table* 1, *col.* 5).—All the compounds except aniline and ethylbenzene absorb at 1082—1065 [1073 ± 4] cm.$^{-1}$; for certain groups the range is less, *e.g.*, olefins absorb at 1073—1069 cm.$^{-1}$, heteroaryl compounds at 1078—1072 cm.$^{-1}$. Split bands and abnormally high intensities occur if a heavy atom is attached directly to the ring. For halogenobenzenes, Randle and Whiffen [12,16] showed that this is because a vibration in which the substituent moves appreciably absorbs in that region for heavy substituents {their values in carbon disulphide are in reasonable agreement with ours: PhCl 1083 cm.$^{-1}$ (109),¶ PhBr 1070 cm.$^{-1}$ (119)}; similar behaviour in other series [1-6] can thus be explained. The intensity is low (10—25) [(15 ± 5)] for weakly conjugating substituents (Nos. 18—66) except for one alcohol (No. 46, strongly overlapped by substituent absorption) and some esters (Nos. 26, 27, 53). Electron-donating (Nos. 1—17) and electron-accepting (Nos. 70—85) substituents cause somewhat higher intensities (10—50) [(25 ± 10)]; esters Nos. 79 and 80 absorb more strongly.

Band Near 1030 *cm.*$^{-1}$ (*Table* 1, *col.* 6).—Compounds with a saturated or olefinic carbon atom next to the ring (Nos. 18—55) absorb at 1030—1025 [1028 ± 1] cm.$^{-1}$ (except No. 50 where the band at 1032 cm.$^{-1}$ is due mainly to substituent absorption); the intensity is low (5—20) [(15 ± 5)] (except Nos. 31, 45, 46 which are strongly overlapped by substituent absorption). Acetylenic substituents cause absorption at 1026—1025 cm.$^{-1}$ (except No. 59, cf. No. 50) (10—15). The position is variable, 1042—1016 cm.$^{-1}$ (10—65), for compounds with another aromatic ring directly attached to the nucleus; similar behaviour occurs in other series often making it difficult to assign bands in this region to a specific aromatic ring. Electron-donating (Nos. 1—17) and electron-accepting (Nos. 70—85) substituents cause absorption at slightly lower frequencies, 1031—1022 cm.$^{-1}$ (5—35) [1026 ± 3 cm.$^{-1}$ (20 ± 10)] and 1030—1021 cm.$^{-1}$ (10—80) [1026 ± 3 cm.$^{-1}$ (35 ± 20)], respectively. The positions and intensities for PhMe 1031 cm.$^{-1}$ (22) ¶; PhEt 1031 cm.$^{-1}$ (18); PhCl 1023 cm.$^{-1}$ (91); PhBr 1021 cm.$^{-1}$ (106) in carbon disulphide [16] solution and the values 1032—1027 cm.$^{-1}$ (20) ¶ [15] for hydrocarbons are in reasonable agreement with our data.

Band Near 1000 *cm.*$^{-1}$.—Most electron-donating groups cause absorption at 1002—990 cm.$^{-1}$ (10—50) (Table 2, col. 3). Compounds with two aromatic rings directly attached to each other {substituent is given: Ph, 1007 cm.$^{-1}$ (*35*); 4-Pyridyl, 1000 (20); 3-Pyridyl, 992 (15); 4-Pyridyl oxide, 999 (10); 3-Pyridyl oxide, 998† (30); 2-Pyridyl oxide, 999 (15)}, the halogenobenzenes {Cl, 1001 cm.$^{-1}$ (10); Br, 998 (45)}, and a few other compounds {CH_2S·4Py, 996 cm.$^{-1}$ (15); CO_2Et, 999 (25)} also absorb in this region.

Band Near 900 *cm.*$^{-1}$.—Most electron-donating substituents cause absorption at 898—860 cm.$^{-1}$ (10—20) (Table 2, col. 4). In addition, absorption is shown in this region for those compounds in which a saturated carbon atom next to the ring carries an oxygen atom {CH_2O·2Py, 905 cm.$^{-1}$ (15); CH_2O·4PyO, 914 (20); CH_2·OH, 905 (10); CH·Ph·OH, 915 (*20*); CH(4Py)OH, 918 (10); CH(2Py)OH, 918 (15)}, for ethynyl substituents {C:C·Ph, 914 (*25*); C:C·4PyO, 915 (15)}, for aminocarbonyl-compounds {CONH·4Py, 885 (15); CONH·3Py, 888 (15); CONH·2Py, 891 (20); CONH·2PyO, 895 (55); CONH·3Py, 874 (10); CONMe·Ph, 874 (15); CONMe·2Py, 883 (10); CONMe·2PyO, 885† (80)}, and for a few other compounds {Ph, 905 (*15*); CN, 922 (15)}. For hydrocarbons, McMurry and Thornton [15] found a band at 909—897 cm.$^{-1}$ (9) ¶.

Substituent Bands.—Absorption bands due to ester, aldehyde, and ketone groups,[9]

¶ Values so marked are converted into ε_A from units used in the original papers.

[16] Randle and Whiffen *Trans. Faraday Soc.*, 1956, **52**, 9.

2-,[3,17] 3-,[1] and 4-substituted pyridine,[2,17] and 2-,[5] 3-,[6] and 4-substituted pyridine 1-oxide[4] rings have been published. All the bands in the spectra of the methyl and ethyl esters (Nos. 26, 27, 34, 35, 52, 53, 79, and 80), benzaldehyde (No. 82), acetophenone (No. 83), and the phenylpyridines and their 1-oxides (Nos. 60—66) have been reported now; bands not correlated (four in the above seventeen compounds) are given in footnotes to the Tables.

In addition to the bands characteristic of the rings, benzylpyridines and their oxides (Nos. 28—32) show shoulders at *ca.* 1430 cm.$^{-1}$ where this region is not obscured {Ph·CH_2·Ph, 1434 * (20); Ph·CH_2·4Py, 1435 * (30); Ph·CH_2·4PyO, 1430 * (30); Ph·CH_2·2PyO 1420 * (50)}; this is possibly the scissor CH_2 vibration displaced from its normal position at *ca.* 1465 cm.$^{-1}$.[10d]

Benzylthio- (Nos. 37—40) and phenylethyl-pyridines and their oxides (Nos. 20—24) show no additional bands (with $\epsilon_A \geqslant 15$) except those at 1106 cm.$^{-1}$ (50) in 4Py·SCH_2Ph which is probably an *X*-sensitive nuclear band of the pyridine nucleus (cf. halides above) and at 1420 * (55) in 2PyO·CH_2·CH_2·Ph which is probably due to the CH_2 group; others are evidently either hidden by the nuclear absorption or have $\epsilon_A < 15$. The α-CH_2 group in 2-substituted pyridine 1-oxides could show abnormal absorption.

Reproducibility of Intensity with Different Machines.—Some spectra were measured at Cambridge, the others at Oxford (see footnote to Table 1). To establish the validity of comparing these spectra, the reproducibility of intensities measured on different instruments was investigated. The spectrum of 4-nitropyridine 1-oxide was measured in duplicate or triplicate using three Perkin-Elmer and two Unicam instruments; ‖ statistical treatment of the intensities gave the results shown in Table 3. Later, a fourth Perkin-Elmer instrument gave intensities which in two runs were (*a*) 0 to 25% [11 ± 7]% and (*b*) −2 to 19 [7 ± 7]% higher than the arithmetical means in Table 4. Thus, apparent extinction coefficients measured under standard conditions, but without any elaborate precautions and with different instruments, are a valuable measure of intensity for diagnostic purposes.

TABLE 3. *Statistical treatment of apparent extinction coefficients.*

Position of band	Range	Arith. mean	Standard deviation	Deviation as % of mean	Position of band	Range	Arith. mean	Standard deviation	Deviation as % of mean
1605 cm.$^{-1}$	195—270	240	23	10	1297 cm.$^{-1}$	370—460	410	23	5
1585	135—160	145	8	6	1286	370—480	435	32	7
1527	210—360	—	—	—[a]	1240	40—45	—	—	—[b]
1517	210—260	240	14	6	1170	105—130	115	9	8
1470	210—300	265	25	9	1120	370—490	430	39	9
1444	25—35	30	4	13	1089	25—50	35	9	26[c]
1353	270—340	310	19	6	1023	65—95	85	8	10
1343	430—540	500	31	6	869	120—180	155	14	9
					852	190—280	230	28	12

[a] This peak not resolved properly on Oxford Perkin-Elmer machine, probably because of wavelength linearity and speed. [b] Peak resolved only on Unicam machines. [c] High standard deviation because one Unicam machine had much higher value.

EXPERIMENTAL

Preparation of Compounds.—The preparations for the pyridines and pyridine 1-oxides have been reported; other compounds were commercial products or were prepared by standard procedures. All compounds were recrystallised or redistilled immediately before measurement.

Measurement of Spectra.—At Oxford, a Perkin-Elmer model 21 instrument was used with an NaCl prism, slit programme 4, and the settings previously reported.[9]

The spectra measured at Cambridge were obtained with a Perkin-Elmer model 21 spectrometer with an NaCl prism and the following settings: gearing, 1 cm. per 100 cm.$^{-1}$ in the

‖ One instrument of another make appeared to give considerably higher results.

[17] R. A. Jones and Katritzky, *J.*, 1958, 3610.

4000—2000 cm.$^{-1}$ region and 4 cm. per 100 cm.$^{-1}$ between 2000 and 600 cm.$^{-1}$; gain 2; other settings as in ref. 9. 0·179M-Solutions in purified chloroform were measured in a 0·112 mm. compensated cell.

Apparent Extinction Coefficients.—In this as in all our previous work, intensities were calculated from $\varepsilon_A = (1/Cl) \log_{10} (I_0/I)$, where C is concentration in moles per litre, and l is cell length in cm.

As solutions were measured at the same concentration and in the same cell, a given percentage absorption always corresponded to the same ε_A, apart from the base-line correction. Measurement of the intensities was facilitated by the construction of a series of rulers for use with different base lines, which permitted ε_A values to be read directly from the graphs.

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838. *Infrared Absorption of Heteroaromatic and Benzenoid Six-membered, Monocyclic Nuclei. Part V.*[1,2] *The Correlation of Intensities of* CC *and* CN *Ring Stretching Frequencies with Charge Disturbance in the Ring.*

By A. R. KATRITZKY.

The intensities of corresponding characteristic modes in the 1600—1400 cm.$^{-1}$ region in benzene, pyridine, pyridine 1-oxide, pyridine–boron trichloride, and their monosubstituted derivatives are compared. The changes in the intensities of the bands from those in benzene are correlated with the charge disturbances created in the ring by the substituents and/or hetero-groups. Agreement is particularly satisfactory for 4-substituted compounds of C_{2v} symmetry.

IN monosubstituted benzenes [1] and pyridines [3-5] and their 1-oxides [6-8] and boron trichloride adducts [9] the intensities of the characteristic bands depend on the nature of the substituent. An explanation for some of these variations is now offered.

Compounds of C_{2v} Symmetry.—Two of the normal vibrations of benzene have frequencies of 1400—1600 cm.$^{-1}$; ν_{16} (I) is infrared-inactive but occurs as a strong band in the Raman

[1] Part IV, Katritzky and Lagowski, preceding paper.
[2] For other related work, see the Series "*N*-Oxides and Related Compounds," Part XV, *J.*, 1958, 3721.
[3] Katritzky and Gardner, *J.*, 1958, 2198.
[4] Katritzky and Hands, *J.*, 1958, 2202.
[5] Katritzky, Hands, and R. A. Jones, *J.*, 1958, 3165.
[6] Katritzky and Gardner, *J.*, 1958, 2192.
[7] Katritzky and Hands, *J.*, 1958, 2195.
[8] Katritzky, Beard, and Coates, unpublished work.
[9] Katritzky, unpublished work.

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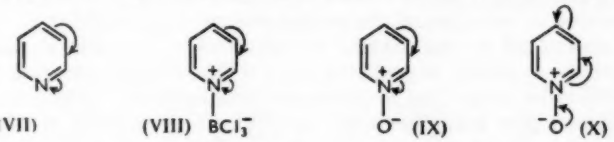
spectrum at 1585 cm.$^{-1}$, and ν_{13} (II) absorbs strongly in the infrared at 1485 cm.$^{-1}$.[10a] These vibrations belong respectively to the symmetry classes E_{2g} and E_{1u}, *i.e.*, they are both doubly degenerate, and when the symmetry is reduced from that of benzene (D_{6h}) to that (C_{2v}) of pyridine, pyridine–boron trihalide, or pyridine oxide, or any of the heterocyclic compounds with a 4-substituent,* or a monosubstituted benzene, each will be split into two frequencies (III—VI). One of each pair belongs to the symmetry class A_1 and is symmetric with respect to the plane of symmetry perpendicular to the ring (III and V); the others (IV and VI) are in the class B_1 and are antisymmetric with respect to this plane.

The following predictions could be made about the intensities of these bands: (i) In compounds in which the combined effect of X and Z is to produce little change in the charge distribution in the ring, vibrations (III) and (IV) should give weak bands (in the infrared) whereas vibrations (V) and (VI) should absorb with an intensity approximately half that in benzene itself. (ii) If X and Z do produce a change in the charge distribution in the ring, this change will be symmetrical with respect to the vertical plane of the molecule and therefore should affect the intensities of vibrations (III) and (V) more than those of (IV) and (VI). However, the relative change in the intensities of (III) and (IV) should be greater than those of (V) and (VI), since the former are allowed only because of the X and Z groups. Thus, intensities should vary with the amount of disturbance of the charge distribution of the ring, strongly in (III), somewhat less in (IV) and (V), and comparatively little in (VI). Moreover, in (III) and (IV) the intensity should increase more or less continuously with increasing charge disturbance, but in (V) the nature of the variation cannot be predicted.

A measure of the effect of a substituent X on the charge distribution in a monosubstituted benzene is given by the mesomeric moment of X (the algebraic difference between the dipole moments of phenyl–X and alkyl–X).[11] The concept of mesomeric moments has been extended by Katritzky and Sutton and their collaborators to include heterocyclic compounds[12,13] and thus measure the effect of the substituent X on these rings. It is more difficult to obtain a precise measure of the effect of Z. Qualitatively, in pyridine (VII) and pyridine–boron trichloride (VIII) electrons are pulled towards Z; in pyridine oxide there are two opposing effects (IX and X). Where Z is $^{+}N{-}O^{-}$ or $^{+}N{-}BCl_3^{-}$, indications are given by taking the difference between the pyridine and tri-



methylamine adducts,[14] but this fails in the case of pyridine and trimethylamine themselves for the dipole moments are very sensitive to small differences of hybridisation of the lone-pair electrons.[14] The pull of electrons in pyridine is certainly less than that in the pyridine–boron trihalide adducts (*ca.* 1·3 D measured as above[14]); we have arbitrarily taken it to be 0·8 D.

The intensity † of an infrared band is determined by the rate of change of dipole

* If the substituent is not symmetrical, this will make little difference to the effectively localised ring vibrations.

† Strictly, integrated areas should be used in intensity correlations; however in many cases they cannot be measured because of band overlap, so apparent extinction coefficients have been used. Large irregularities in the half-band widths were not observed.

[10] Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules," Van Nostrand, New York, 1945, (*a*) p. 364, (*b*) p. 241.
[11] Everard and Sutton, *J.*, 1951, 2818, and references therein.
[12] Katritzky, Randall, and Sutton, *J.*, 1957, 1769.
[13] Bax, Katritzky, and Sutton, *J.*, 1958, 1254.
[14] *Idem*, *J.*, 1958, 1258.

moment with the normal co-ordinate at the equilibrium position, *i.e.*, $\partial\mu/\partial Q$. The dipole moment of a covalent bond must reach a maximum at some internuclear distance, for it will be zero when the two atoms are infinitely near to each other or far apart.[10b] Thus, strictly, no conclusion regarding $\partial\mu/\partial Q$ can be drawn from a knowledge of the value of μ in the direction Q at the equilibrium position. However, in a series of closely related molecules, it might well be true that $(\partial\mu/\partial Q)^{2*}$ increases continuously as some function of μ_Q.

For a qualitative comparison of the results with the predictions, substituents have been divided into three main types: (*a*) strong electron-donors, including substituted amino- and alkoxy-groups for which the average mesomeric moment has been taken as the mean of that of the dimethylamino- and methoxy-compound in each group, (*b*) substituents with a saturated carbon atom directly attached to the nucleus, which are usually weakly electron-donating and for which the mesomeric moment has been taken as that of the particular methyl compound, and (*c*) strong electron-acceptors with a carbonyl or nitro-group directly attached to the nucleus, for which the mesomeric moment has been taken as the mean of the ethoxycarbonyl, acetyl and nitro-compounds. Mean values of apparent extinction coefficients for these types of substituent (taken from refs. 1, 3, 6, 9) are given in Table 2, and average values for the disturbance of charge distribution in the ring in Table 1. Compounds with halogen or unsaturated carbon atoms directly attached to the nucleus are not included, since these substituents can be both electron donors and acceptors.

TABLE 1. *Disturbance of charge distribution in ring (Debyes).*

Type of subst.	Monosubst. benzene	4-Subst. pyridine	4-Subst. pyridine 1-oxide	4-Subst. pyridine–boron trichloride
Donor	1·3	2·5	1·2	2·6
Weak	0·3	1·2	0·3	2·0
Nil	0	0·8	0·8	1·3
Acceptor	0·6	0·4	1·6	1·1

As predicted, vibration (VI) shows (Table 2, Entries 13—16) the least variation in apparent extinction coefficients: X has little effect, Z somewhat more. Vibration (III) shows intensity variations (Table 2, Entries 1—4) which are qualitatively in good agreement with the variations in the value of charge disturbance given in Table 1. Vibration (IV) is absent or unresolved in the oxides; in the other compounds it shows intensities (Table 2, Entries 5—8) which, as predicted, are less than those of vibration (III) but are in the same relative order except that pyridines and pyridine–boron trichlorides with acceptor substituents show higher intensities than expected. The variation of vibration (V) was expected to show less correlation with the values in Table 1; it appears to become intense when any electron-donating group (including *N*-oxide) is attached to the ring.

In an attempt at quantitative correlation, extinction coefficients for the A_1 band near 1600 cm.$^{-1}$ have been plotted against the disturbance to charge distribution in the ring (Figure); there is a trend, but much scatter. The scatter is not surprising in view of the nature of the treatment and the approximations and assumptions involved.

Compounds of C_s Symmetry.—In the 2- and 3-substituted compounds the normal co-ordinates of the ring vibrations are not uniquely determined (lower symmetry), and the two charge disturbances are not collinear, cannot be algebraically added, and have no directional relation to the normal co-ordinates. Also no mesomeric moments are available.

However, intensity variations with the substituent type (Table 3) can be accounted for approximately. Replacement of H by a substituent changes masses and force constants more than replacing CH by N; thus a 2- or 3-substituted pyridine has effective C_{2v} symmetry, and in-plane vibrations are A_1 or B_1 according to their symmetry about

* If the square is considered, the sign of $\partial\mu/\partial Q$ does not matter, and intensities are proportional to $(\partial\mu/\partial Q)^2$.

TABLE 2. *Mean positions and apparent extinction coefficients of bands in C_{2v} compounds.*

No.	Type of subst.	Monosubst. benzene [a] cm.$^{-1}$	ε_A	4-Subst. pyridine [b] cm.$^{-1}$	ε_A	4-Subst. pyridine 1-oxide [c] cm.$^{-1}$	ε_A	4-Subst. pyridine boron trichloride [d] cm.$^{-1}$	ε_A
	A_1 Vibration near 1600 cm.$^{-1}$ (III)								
1	Donor	1603	200	1599	385	1636	85	1640	270
2	Weak	1605	15	1606	150	1622	5	1640	175
3	Hydrogen	1585 [e]	0	1588	60	1612	50	1630	90
4	Acceptor	1604	50	1602	30	1613	170	1640	90
	B_1 Vibration near 1580 cm.$^{-1}$ (IV)								
5	Donor	1586	60	1569	85	—		1568	75
6	Weak	—		1563	20	—		1561	15
7	Hydrogen	1585 [e]	0	(—)		—		(—)	
8	Acceptor	1585	35	1567	50	—		1569	
	A_1 Vibration near 1500 cm.$^{-1}$ (V)								
9	Donor	1498	155	1507	155	1489	275	1511	160
10	Weak	1495	40	1495	10	1485	195	1505	25
11	Hydrogen	1481	40 [f]	1481	15	1468 †	280	1490	30 [f]
12	Acceptor	1489	15	1490	10	1480	110	(—)	
	B_1 Vibration near 1440 cm.$^{-1}$ (VI)								
13	Donor	1451	30	1421	35	1436	60	1460	75
14	Weak	1454	45	1417	75	1447	60	1448	135
15	Hydrogen	1481	40 [f]	1439	75	1468 †	280	1461	140 [f]
16	Acceptor	1451	55	1411	100	1442	90	1430	190

Values for benzene, pyridine, and pyridine 1-oxide were obtained by measurements in chloroform solution under the usual standard conditions; [1] the assignments agree with those given by other workers.

† Indicates peak formed by the superimposition of two bands, (—) indicates band is hidden, — indicates apparent absence of band.

[a] From Ref. 1. [b] From Ref. 3. [c] From Ref. 6. [d] From Ref. 9. [e] Frequency from Raman spectrum.[10a] [f] Mean value for pyridine–boron trihalide complexes.[9] [g] The ε_A (80) given by Jones and Sandorfy (in Weissburger, "Technique of Organic Chemistry. Vol. IX. Chemical Applications of Spectroscopy," Interscience Publ. Inc., London, 1956; p. 397) has been halved to take into account the twofold degeneracy of this band in benzene. We found ε_A (70) in benzene.

TABLE 3. *Mean positions and apparent extinction coefficients in bands of C_s compounds.*

No.	Type of subst.	3-Subst. pyridine [a] cm.$^{-1}$	ε_A	2-Subst. pyridine [b] cm.$^{-1}$	ε_A	3-Subst. pyridine 1-oxide [c] cm.$^{-1}$	ε_A	2-Subst. pyridine 1-oxide [d] cm.$^{-1}$	ε_A
	A_1 Vibration near 1600 cm.$^{-1}$								
1	Donor	1592	100	1600	170		[e]	1620	160
2	Weak	1598	15	1596	105	1609	90	1615	15
3	Acceptor	1597	140	1589	75	1608	45	1608	45
	B_1 Vibration near 1580 cm.$^{-1}$								
4	Donor	1579	70	1577	160		[e]	1572	200
5	Weak	1581	40	1572	50	1564	25	—	
6	Acceptor	1580	20	1573	35	1567	25	1536	15
	A_1 Vibration near 1500 cm.$^{-1}$								
7	Donor	1483	165	1474	200		[e]	1500	190
8	Weak	1479	50	1475	70	1483	95	1490	125
9	Acceptor	—		1467	20	1476	50	1483	25
	B_1 Vibration near 1440 cm.$^{-1}$								
10	Donor	1429	115	1435	250		[e]	1439	200
11	Weak	1422	65	1434	65	1434	130	1443	175
12	Acceptor	1422	70	1435	50	1437	170	1431	215

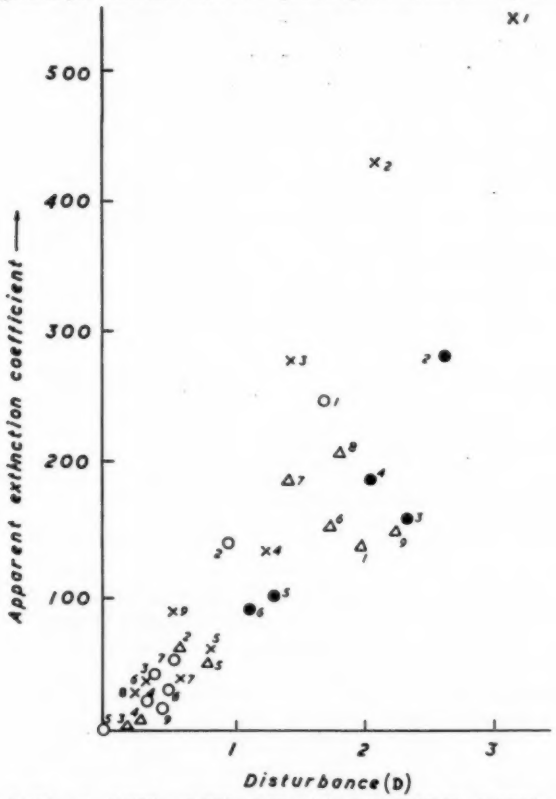
[a] From Ref. 5. [b] From Ref. 4. [c] From Ref. 8. [d] From Ref. 7. [e] Not yet available.

lines as in (XI) and (XII). 3-Substituents in pyridine are chemically similar to those in benzene, but 2-substituents to those in the 4-position; [15] *i.e.*, both electron-attracting and -donating groups conjugate in the 3-position but only the latter effectively in the 2-position

[15] Cf., *e.g.*, Mosher in Elderfield, "Heterocyclic Compounds," Wiley, New York, 1950, Vol. 1, Chap. 8.

(cf. the C:O, C·O, and C·N frequencies of carbonyl groups,[16] ethers,[17] and amines[18]). Charge disturbance by the substituent is in the direction of the vibration near 1600 cm.$^{-1}$, and these intensities (Table 3, Nos. 1—3) are explained by varying conjugation of the substituent and a constant influence of the nitrogen atom. Intensity variation is less for the band near 1580 cm.$^{-1}$ (Table 3, Nos. 4—6) as expected. The E_{1u} vibration of benzene

Extinction coefficients for band near 1600 cm.$^{-1}$ plotted against disturbance of charge symmetry.



Numbers refer to substituent: 1 NMe_2, 2 OMe, 3 Cl, 4 Me, 5 H, 6 CO_2Et, 7 COMe, 8 NO_2, 9 CN.
Ring systems are represented: ○ Benzene, × Pyridine, △ Pyridine oxide, ● Pyridine–boron trichloride.
Nitrobenzene is not included because the band is split into two components in this compound.

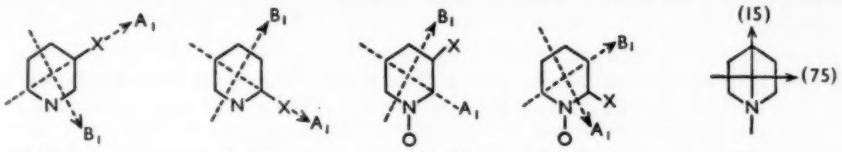
at 1485 cm.$^{-1}$ (2 × 40) is split in pyridine as shown (XV). With normal co-ordinates symmetrical about directions intermediate to those in (XV) the nitrogen atom should have little effect on the intensities, which for the bands near 1500 and 1440 cm.$^{-1}$ in 2- and 3-substituted pyridines (Table 3, Nos. 7—12) are indeed similar to those of the corresponding benzenes, except that the B_1 band intensities are also increased by donor groups.

The 2- and 3-pyridine 1-oxides will also have approximate C_{2v} symmetry (XIII) and (XIV), both the $^+N{-}O^-$ and substituent influencing all the vibrations. Data in Table 2 indicate that those near 1600 and 1580 cm.$^{-1}$ should be affected mainly by the substituent

[16] Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[17] Katritzky and Coates, unpublished work.
[18] Katritzky and R. A. Jones, unpublished work.

XUM

and those near 1500 and 1440 cm.$^{-1}$ by the $^{+}N{-}O^{-}$ group. The 3-pyridine 1-oxide ring conjugates effectively only with electron-donor substituents,[16] in agreement with the intensity variation observed. The 2-pyridine 1-oxide ring, already known to conjugate



(XI) (XII) (XIII) (XIV) (XV)

strongly with electron donors,[17,18] is now indicated to conjugate also with acceptors (cf. refs. 16 and 19). The appreciable intensity of the 1500 and 1440 cm.$^{-1}$ bands is explained by the influence of the $^{+}N{-}O^{-}$ group.

We thank Dr. N. Sheppard for discussion and advice, and Dr. J. M. Lagowski for help in the preparation of the manuscript. Part of this work was done during the tenure of an I.C.I. Fellowship.

University Chemical Laboratory, Cambridge.
Dyson Perrins Laboratory, Oxford. [*Received, May 19th*, 1958.]

[18] Hands and Katritzky, *J.*, 1958, 1754.

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839. *An Electrometric Method for Measuring the Thickness of the Air-formed Oxide Film on Pure Iron and Mild Steel.*

By P. Hancock and J. E. O. Mayne.

A method has been developed of estimating the thickness of the air-formed oxide film on pure iron and mild steel. The film was cathodically reduced in deaerated 0·2N-potassium chloride and the thickness of the film calculated from the quantity of electricity consumed. Sources of error were examined, and the method was confirmed gravimetrically. The air-formed film on pure iron and mild steel was between 26 Å and 40 Å thick, depending upon the surface condition.

The thickness of the air-formed oxide film on iron was first obtained electrometrically by Miley and Evans,[1] who determined the number of coulombs required to reduce the film when immersed in ammonium chloride solution in an open beaker, as between 170 and 210 Å. However, more recent measurements by other methods [2] yielded much lower values, *i.e.*, 20—40 Å. (Thicknesses were expressed in Å/apparent cm.^{2}.)

We have now reassessed the electrometric method. It was felt that an improved technique might yield results closer to those from other methods, and be useful for investigating inhibition (following paper).

Campbell and Thomas,[3] investigating oxide and sulphide films on copper, greatly improved the cathodic reduction method by deaerating their electrolyte, potassium chloride, and using very small current densities, which permitted accurate measurements of the time of reduction. Kubanov and Leikis [4] cathodically reduced the air-formed film on iron in 2N-sodium hydroxide, in absence of air, but the potential–time curve had no arrest corresponding to the reduction of the oxide film.

[1] Miley and Evans, *J.*, 1937, 1295.
[2] Gulbransen, *Trans. Electrochem. Soc.*, 1942, **82**, 375; Winterbottom, *J. Iron Steel Inst.*, 1950, **165**, 9; Sloman, Eighth Report on the Heterogeneity of Steel Ingots, Iron and Steel Inst., Special Report No. 25, 1939, p. 60.
[3] Campbell and Thomas, *Trans. Electrochem. Soc.*, 1939, **76**, 303.
[4] Kubanov and Leikis, *Acta Physicochim., U.R.S.S.*, 1946, **21**, 769.

The electrometric method is open to three sources of error: (1) If deaeration of the electrolyte is insufficient, oxygen will be reduced with the oxide; (2) the electrolyte may attack the film before or during the measurement; (3) all the oxide may not be reduced; this may occur if the film contains magnetite (magnetite produced on iron at 250° cannot be reduced [5]).

We examined the cathodic reduction of the air-formed film on iron and mild steel in 0·2N- and 0·1N-ammonium chloride, 0·1N-sodium hydroxide, and 0·2N-potassium chloride, with two methods of deaeration. Both ammonium chloride solutions rapidly removed the film and attacked the metal, irrespective of the method of deaeration; when the deaeration was very efficient the film was removed by sodium hydroxide and potassium chloride attacked the film very slowly. However, attack by potassium chloride was negligible provided that the current was applied as soon as the iron specimen touched the solution. The effect of the surface condition of the specimens and the chemistry of the reduction process were examined and the fact that all the film substance was reduced confirmed by means of a microbalance. The thicknesses of the air-formed films on pickled iron, hydrogen-reduced iron, and pickled mild steel were estimated.

Experimental

Materials.—Iron contained C, 0·0036; Si, 0·001; Mn, 0·005; S, 0·0057; Al, 0·001; O_2, 0·0024; N_2, 0·0016%, and was in sheets 0·018 in. thick. Mild steel contained C, 0·06; S, 0·021; P, 0·015; Mn, 0·36; Ni, 0·048; Cu, 0·04; Sn, 0·008 wt. %; Si, trace only, and was in sheets 0·016 in. thick.

Specimens.—Pickled. The specimens, 2 × 1 cm., degreased by swabbing in benzene, then acetone, were pickled in dilute hydrochloric acid (1 : 4 acid : water) at 20° for 20 sec., washed in six portions of absolute alcohol, dried quickly on filter paper, and stored in a desiccator ($CaCl_2$) for 48 hr.

Hydrogen-reduced. Specimens, swabbed with benzene and acetone and allowed to dry, were placed in the apparatus shown in Fig. 1. The furnace was evacuated to 10^{-5} mm. Hg by a three-stage mercury-diffusion pump; the temperature was raised to 380° and hydrogen, at just below atmospheric pressure, admitted and left in contact with the specimens for ½ hr. The furnace was again evacuated, the temperature raised to 460°, and hydrogen re-admitted and kept with the specimens for 1 hr. The furnace was cooled to room temperature and again evacuated. Air was admitted slowly and the specimens were removed and stored in a desiccator ($CaCl_2$) for 48 hr.

Apparatus.—In preliminary experiments difficulty was experienced in maintaining good electrical contact between the specimen and the platinum hook (*F* in Fig. 3). This was overcome by suspending the specimen as shown in Fig. 2 *B*(ii), which was superior to the system shown in Fig. 2 *B*(i) since the specimen made contact at two points. The glass bead was used to weight the specimen and immediately before an experiment the iron wire was scraped at the point where it made contact with the platinum.

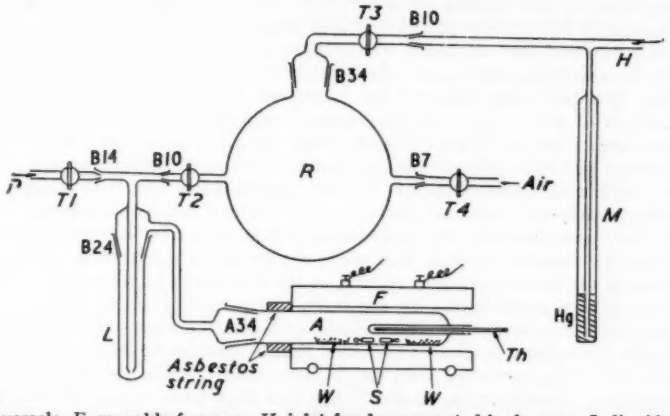
Two methods of deaerating the electrolyte were examined. The first consisted of alternately freezing and thawing the solution under vacuum,[6] and the second was similar to that used by Mills and Willis.[7] The apparatus is shown in Fig. 3. The solution was contained in flask *A* and the specimen was suspended from the platinum hook *F*. Vessels *A* and *B* were evacuated through *C* until the solution boiled, tap *D* was then opened for a few minutes to evacuate directly the reaction vessel *B*. Taps *C* and *D* were closed and oxygen-free hydrogen was admitted through *E* into *B* and bubbled into *A* through the solution. This cycle was repeated seven times, after which the solution was blown into *B* to the desired level by admitting hydrogen into *A* by tap *G*, the flow being stopped by opening *D* to equalise the pressures in *A* and *B*. After the reaction vessel was charged with electrolyte a pressure of 1 atm. of hydrogen was maintained in the apparatus to minimise air leakage into the cell, and to prevent appreciable change of the partial pressure of hydrogen above the iron specimen during reaction.

[5] Davies, Evans, and Agar, *Proc. Roy. Soc.*, 1954, *A*, **225**, 443; Buob, Beck, and Cohen, *J. Electrochem. Soc.*, 1958, **105**, 74.
[6] Mayne and Menter, *J.*, 1954, 100.
[7] Mills and Willis, *J. Electrochem. Soc.*, 1953, **100**, 452.

The caps H and H_1 were of soda-glass with standard ground-glass joints; sealed through the top of each was a platinum hook. One of these was used as an anode to supply constant current to the iron specimen, a standard Ag/AgCl electrode being suspended from the other.

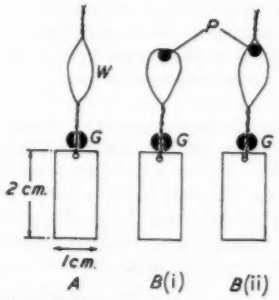
Whilst the electrolyte was being deaerated the specimen was held in the position shown in Fig. 3 by an external magnet. After the reaction chamber was filled, the specimen was dropped

FIG. 1.



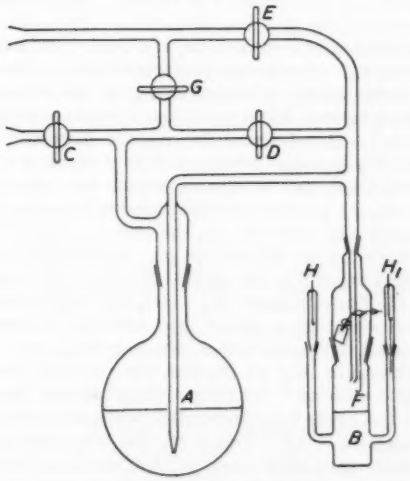
A, Reaction vessel; *F*, movable furnace; *H*, inlet for deoxygenated hydrogen; *L*, liquid-air trap; *M*, manometer; *P*, connection to pumps and McLeod gauge, *via* liquid-air trap; *R*, 7 litre hydrogen reservoir; *S*, specimens; *Th*, thermometer; *W*, platinised asbestos wad.

FIG. 2.



G, Glass bead.
P, end section of platinum wire hook.
W, pure iron wire.

FIG. 3.



into the solution and the cathodic reduction begun immediately. The effect of the electrolyte on the film was thus minimised. The potential of the specimen was measured against the Ag/AgCl electrode on a " Cambridge " valve potentiometer, readings being taken every 15 sec.

Development of Method.—Pickled iron specimens were cathodically polarized in 0·2N and 0·1N-ammonium chloride deaerated by both methods, at 10—40 μA/cm.². The potential always fell as soon as the current was applied and after 0·1—0·2 mc had passed became constant. A large pickled specimen, 10 × 1 cm., was left in contact with 0·1N-ammonium chloride, which

had been deaerated by seven cycles of freezing and thawing, for 15 min. The specimen was then removed from the solution magnetically and the vacuum broken; the iron content of the solution, estimated colorimetrically with thioglycollic acid, was 100 μg. If the air-formed film is taken to be 40 Å thick and assumed to consist of γ-Fe_2O_3, then the total film on 20 cm.^{2} would contain only 28 μg. of iron. Deaerated ammonium chloride must both rapidly dissolve the air-formed film and attack the iron.

When 0·1N-sodium hydroxide was used the cathodic potential–time curves showed definite arrests, irrespective of the method of deaeration. In some experiments with 0·1N-sodium hydroxide, deaerated by 7 cycles of freezing and thawing, the specimens behaved as if they carried no oxide film and this conclusion was confirmed by the shape of the anodic polarization curves, which showed three arrests and were similar to those obtained with iron [6] from which the air-formed film had been removed by treatment with acid. Attempts to detect the calculated amount of iron in solution were unsuccessful, but it was concluded that sodium hydroxide may attack the oxide film provided that the solution is highly deaerated.

0·2N-Potassium chloride yielded potential–time curves with definite arrests, which corresponded very well with those obtained in most experiments with 0·1N-sodium hydroxide. Both methods of deaeration were satisfactory. No evidence was obtained that the film was severely attacked; unfortunately, the estimations of iron were near the limit of sensitivity of the method, but the results suggested that when the specimen was kept with deaerated 0·2N-potassium chloride for 30 min. as much as 20% of the film might be dissolved. This was why the current was applied immediately the specimen touched the solution.

The general conclusions were that both methods of deaeration were satisfactory for potassium chloride, and also for sodium hydroxide provided that deaeration by freezing and thawing was not carried too far. However since Mills and Willis's method [7] was quicker it was adopted as standard procedure. Furthermore, it was concluded that ammonium chloride was an unsuitable electrolyte, since it removed the oxide film; and that either 0·2N-potassium chloride or 0·1N-sodium hydroxide could be used, but that potassium chloride was preferable, since the Ag/AgCl electrode is more reproducible than the Ag/Ag_2O electrode.

The effect of the surface condition of the iron specimen was examined in both 0·2N-potassium chloride and 0·1N-sodium hydroxide. Reproducible end-points were obtained with specimens reduced in hydrogen, and also with specimens pickled with standardized times and temperatures. Specimens prepared in either manner yielded concordant results when reduced in both electrolytes. Specimens electropolished in acetic anhydride–perchloric acid gave very irreproducible results, probably owing to variables in the technique of electropolishing; this was not investigated further. Cathodic reduction curves obtained with abraded specimens had no arrests, possibly because the oxide is shattered and may contain magnetite owing to the high surface temperature produced during abrasion.

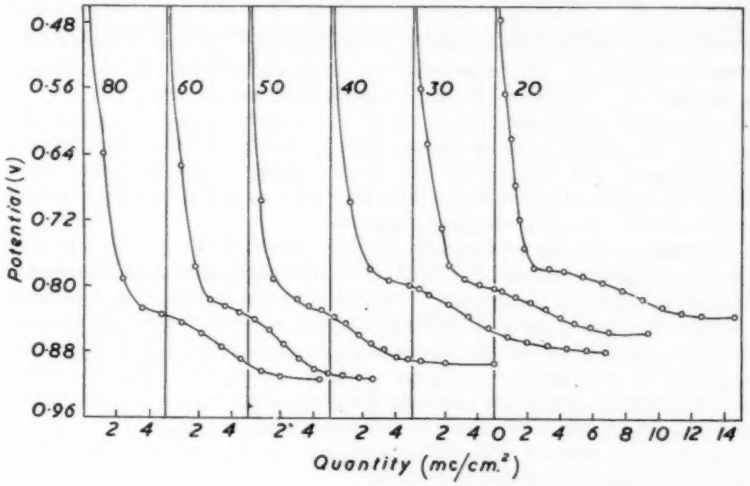
The chemistry of the reduction was next examined. A large specimen, 40 cm.^{2}, was cathodically polarized in deaerated 0·2N-potassium chloride for 20 min. at 40 μA/cm.^{2}. The specimen was removed and the iron in solution determined. In two experiments the solution contained 7·5 μg. of iron, but in a third no iron was detected. It was found subsequently that the air-formed film on pickled iron required about 7 mc for reduction. On the assumption that the film consisted of γ-Fe_2O_3 and was reduced only to the ferrous condition, then 160 μg. of iron would have passed into solution. Consequently it was concluded that the oxide was converted during reduction into metallic iron.

To ensure that all the film was reduced, the results obtained by cathodic reduction were checked with an " Oertling " microbalance, sensitive to ±3 μg. For each experiment eight small specimens were prepared for cathodic reduction and three large specimens 7·5 cm. × 4 cm. for weighing. After degreasing the large specimens were adjusted in weight to within 200 μg. by filing, again degreased, pickled, dried on filter paper, stored overnight in a desiccator, and adjusted to within 20 μg. The heaviest specimen was kept as a standard; the other two were used in the experiment.

The two large specimens and the eight small specimens were heated in an oven at 70° to remove adsorbed gas. After cooling in a desiccator, the large specimens were weighed against the standard and four small specimens were cathodically reduced. The two large specimens and the four remaining small specimens were then heated to a given temperature between 120° and 200°, then cooled in a desiccator. The large specimens were reweighed, the small specimens cathodically reduced, and the increase in weight obtained with the large specimens compared

with the difference in weight calculated from the cathodic reduction curves. Four experiments, in which the final heating temperatures were 130°, 160°, 170°, and 200°, gave measured and calculated values in good agreement. Averaging the errors, we found that the increase in weight due to oxygen as calculated from the cathodic reduction curves was 3·5% greater than the increase as measured by the microbalance, so the whole film was reduced during cathodic treatment.

FIG. 4. *Cathodic reduction of air-formed film on iron at the current densities (μA/cm.²) shown on the curves. The potential is given against the normal hydrogen electrode.*



Estimation of the Thickness of the Air-formed Film.—When pickled, or hydrogen-reduced, iron or mild steel was cathodically reduced in deaerated 0·2N-potassium chloride the potential first fell to that at which the entire oxide film was reduced to metal and then dropped to the potential of hydrogen evolution. The end-point in the curve was taken as the midpoint between the potential of the arrest and the potential of hydrogen evolution; this end-point invariably corresponded to the point of inflexion on the potential–time curve. The thickness of the oxide film was calculated from the number of coulombs required for reduction, the film being assumed to consist of γ-Fe_2O_3 of specific gravity 5 (see Table).

Current density (μA/cm.²)	Arrest potl. (mv)	Potl. of H_2 evoln. (mv)	Electricity to reduce film (mc/cm.²)	Thickness of film (Å/apparent cm.²)
Pure iron, pickled				
20	−780	−836	7·5	41·5
30	−800	−856	7·5	41·5
40	−800	−880	7·5	41·5
50	−826	−896	6·8	38
60	−826	−914	7·2	40
80	−834	−914	7·5	41·5
Average	—	—	7·3	40
Mild steel, pickled				
40	−790	−863	6·5	36
40	−790	−866	6·7	37
Average	−790	−865	6·6	36·5
Pure iron, hydrogen-reduced				
40	−790	−890	4·2	23
40	−790	−880	4·4	24
40	−790	−878	4·8	27
40	−788	−890	5·3	29
40	−790	−880	4·8	27
Average	−790	−884	4·7	26

The results obtained when pickled iron was reduced at 20—80 μA/cm.² are shown in Fig. 4 and the Table. The higher the current density, the sharper the end-point, but if too high the time of reduction becomes inconveniently short. The optimum value was taken to be 40 μA/cm.², as used for the other materials.

DISCUSSION

Iron exposed to air becomes covered with an oxide film, first isolated by Evans.[8] Several workers have determined the composition by electron diffraction,[9] and have found that it consisted of an anhydrous cubic oxide, Fe_3O_4, γ-Fe_2O_3, or an intermediate compound. Davies, Evans, and Agar [5] could not cathodically reduce magnetite, produced by heating iron at 250° and above; furthermore, Evans and Davies [10] produced evidence supporting the view that the air-formed film contains at least 80% of γ-Fe_2O_3. Consequently, we calculated the thickness on the assumption that the film consisted of γ-Fe_2O_3.

The thickness of the air-formed film on pickled pure iron is independent of the current density used to reduce it. As the period of reduction varied from 4 to 16 min. we conclude that during this time the electrolyte had no appreciable action on it.

Good end-points were obtained in most experiments with 0·1N-sodium hydroxide, provided that the current was applied as soon as the specimen made contact with the solution; Kubanov and Leikis [4] did not obtain arrests when specimens carrying air-formed films were cathodically reduced; this may have been due to attack on the film due to delay, or to their use of 2N-sodium hydroxide.

The thickness of the air-formed film on pickled iron is 40 Å, on pickled mild steel 36·5 Å, and on hydrogen-reduced iron 26 Å. The last result is in good agreement with the value of 29 Å obtained by Gulbransen [2] when pure iron was reduced in hydrogen and the loss in weight determined by a microbalance; Winterbottom,[2] using an optical method, concluded that the thickness of the air-formed film on carbonyl iron was between 20 and 40 Å according to the surface condition; Sloman,[2] using the vacuum fusion method, measured the surface oxygen on cold-rolled but unabraded pure iron and obtained the value of 0·56 $\mu g/cm.^2$, which corresponds to a film thickness of 37 Å.

The electrometric method, with precautions, is thus useful for measuring the thickness of the air-formed film on iron and mild steel.

The authors thank Mr. C. A. J. Taylor for preparing diagrams for this and the following paper.

DEPARTMENT OF METALLURGY,
UNIVERSITY OF CAMBRIDGE. [*Received, May 20th*, 1958.]

[8] Evans, *J.*, 1927, 1020.
[9] Mayne and Pryor, *J.*, 1949, 1831.
[10] Evans and Davies, *J.*, 1956, 4373.

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840. *The Effect of Inhibitors of the Corrosion of Iron on the Air-formed Film.*

By P. HANCOCK and J. E. O. MAYNE.

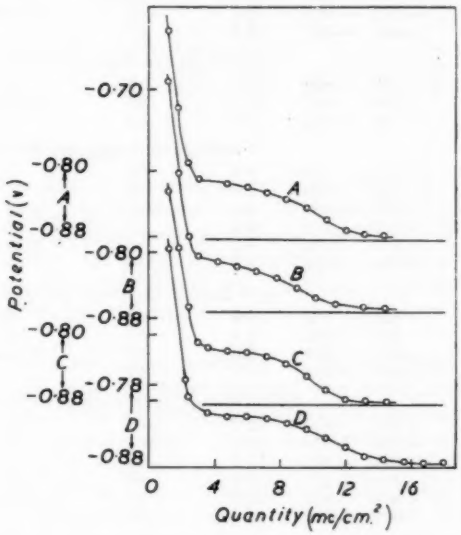
The effect of 0·1N-sodium benzoate, acetate, borate, carbonate, and hydroxide on the air-formed film on pickled mild steel, pickled iron, or iron reduced in hydrogen, was determined electrometrically.

The air-formed film was reinforced and thickened by material of similar composition to the extent of 20—120%, depending upon the inhibitor and the surface condition of the metal.

IRON or mild steel exposed to air becomes covered with an oxide film 26—40 Å thick [1] which is always permeable to iron ions, since however long iron may have been in contact with the air, it always corrodes when immersed in water. But when iron, carrying its air-formed film, is immersed in 0·1N-sodium hydroxide, carbonate, borate, acetate, or benzoate it does not corrode, indicating a change in the permeability of the oxide film.

[1] Hancock and Mayne, preceding paper.

The composition of the film formed by these inhibiting solutions has been established. The air-formed film was first removed from iron specimens with dilute acid, the acid was then displaced by a large volume of the inhibiting solution,[2] which was saturated with air, and the iron was left in contact with the solution for 1—2 days. The film was then removed and shown by electron diffraction to be an anhydrous cubic oxide of similar composition to that of the air-formed film. It was concluded that the anhydrous cubic oxide was derived from the inhibitive ions in solution, but later it was thought that the air-formed film might have been rapidly re-formed by the air dissolved in the solution; inhibition might then have occurred owing to repair of weak spots in the air-formed film by oxidation of insoluble compounds derived from the inhibitive anions.[3] If the final film



Potentials are on the hydrogen scale.
A, Sodium benzoate.
B, Sodium borate.
C, Sodium carbonate.
D, Sodium hydroxide.

contained less than 10% of these compounds they might not have been detected by electron diffraction and the oxide film would not have been appreciably thickened by the inhibiting solutions.

The thickness of the films on iron and mild steel before and after treatment with inhibiting solutions has now been measured electrometrically.[1]

Experimental

Compositions of iron and mild steel and methods of pickling or reduction in hydrogen were as before.[1]

The specimens were pickled or reduced simultaneously, then stored in a desiccator ($CaCl_2$) for 24 hr., then totally immersed in the inhibiting solutions. At intervals during 1—18 days, specimens were withdrawn, washed six times with absolute alcohol, dried on filter paper, and cathodically reduced. Experiments with sodium acetate and iron were done later, but as nearly as possible under the same conditions.

Cathodic reductions were carried out in 0·2N-potassium chloride, deaerated by six cycles of flushing and boiling under vacuum. The constant current density was 40 μA/cm.[2] and potentials were measured every 15 sec.

[2] Mayne, Menter, and Pryor, *J.*, 1950, 3229; Mayne and Menter, *J.*, 1954, 99 (NaOH), 103 (Na_2CO_3, $Na_2B_4O_7$); Menter, unpublished work (NaOAc); Chemistry Research, 1950, H.M.S.O., London, 1951, p. 19 (NaOBz).

[3] Mayne, *Chem. and Ind.*, 1953, 538.

Results for pickled iron are given in Table 1 and a typical set of potential–time curves for four inhibiting solutions is shown in the Figure. Tables 2 and 3 give the results obtained with pickled mild steel and hydrogen-reduced iron.

TABLE 1. *Pickled iron.*

t [a] (days)	A [b] (mv)	H_2 [c] (mv)	Q [d] (mc/cm.²)	F [e] (Å/appar. cm.²)	t [a] (days)	A [b] (mv)	H_2 [c] (mv)	Q [d] (mc/cm.²)	F [e] (Å/appar. cm.²)
0·1N-Sodium benzoate, pH 7·1; thickening [f] 40%									
1	−818	−888	8·5	47	9	−828	−874	9·6	53
1	−820	−866	9·0	50	16 *	−832	−886	10·9	61
1	−820	−880	9·5	53	16 *	−838	−888	12·3	68
2	−825	−872	9·6	53	18 *	−830	−892	11·4	63
3	−812	−868	9·6	53	Average	−824	−880	10·05	56
5	−820	−882	10·2	57					
0·1N-Sodium acetate, pH 8·42; thickening 40%									
1	−825	−890	10·0	56	4	−827	−872	10·0	56
1	−804	−860	10·8	60	Average	−819	−874	10·1	56
1	−820	−874	9·6	53					
0·1N-Sodium borate, pH 9·2; thickening 35%									
1	−812	−876	10·8	60	5	−810	−880	8·8	49
1	−814	−868	9·0	50	15	−818	−870	10·0	56
1	−810	−890	8·5	47	15	−818	−874	11·3	63
2	−812	−870	9·8	55	18	−818	−872	11·0	61
2	−818	−886	8·7	48	Average	−814	−877	9·7	54
3	−810	−880	8·9	50					
0·1N-Sodium carbonate pH 11·0; thickening 37%									
1	−826	−893	8·8	49	9	−825	−863	10·2	57
1	−822	−882	9·5	53	11	−828	−903	10·8	60
2	−829	−890	9·6	53	Average	−828	−886	9·9	55
9	−835	−886	10·3	57					
0·1N-Sodium hydroxide, pH 12·5; thickening 59%									
1	−818	−874	12·2	68	2	−816	−870	11·4	53
1	−820	−876	11·0	61	3	−825	−885	11·4	63
1	−826	−878	11·2	62	8	−816	−850	11·8	66
1	−818	−864	10·8	60	9	−820	−868	13·0	72
1	−816	−860	10·8	60	Average	−820	−870	11·4	63·5
2	−827	−876	11·0	61					

[a] Time in inhibitor (days). [b] Arrest potential. [c] Potential of evolution of hydrogen. [d] Quantity of electricity required to reduce the film. [e] Thickness of film to nearest Å. [f] Increase in film thickness due to action of inhibitor. All potentials are on the hydrogen scale.

* Mould in solution.

TABLE 2. *Pickled mild steel.*

t (days)	A (mv)	H_2 (mv)	Q (mc/cm.²)	F (Å/appar. cm.²)	t (days)	A (mv)	H_2 (mv)	Q (mc/cm.²)	F (Å/appar. cm.²)
0·1N-Sodium benzoate, pH 7·1; thickening 40%									
2	−784	−890	9·0	50	3	−808	−904	9·5	53
2	−784	−910	9·5	53	Average	−800	−903	9·2	51
3	−815	−908	8·7	48					
0·1N-Sodium borate, pH 9·2; thickening 18%									
2	—	−922	7·8	43	5	−800	−932	7·6	42
3	−760	−895	7·5	42	Average	−783	−912	7·8	43
3	−790	−900	8·2	46					
0·1N-Sodium carbonate, pH 11·0; thickening 23%									
1	−784	−916	7·2	40	3	−805	−925	8·5	47
2	−800	−926	7·5	42	5	−830	−932	9·2	51
3	−783	−910	8·4	47	Average	−800	−922	8·1	45
0·1N-Sodium hydroxide, pH 12·5; thickening 56%									
1	−802	−914	9·1	51	3	−807	−921	9·4	52
2	−814	−908	11·4	63	3	−820	−913	11·4	63
3	−803	−905	10·0	56	Average	−809	−912	10·3	57

TABLE 3. *Hydrogen-reduced iron.*

t (days)	*A* (mv)	H_2 (mv)	*Q* (mc/cm.²)	*F* (Å/appar. cm.²)	*t* (days)	*A* (mv)	H_2 (mv)	*Q* (mc/cm.²)	*F* (Å/appar. cm.²)
0·1N-Sodium benzoate, pH 7·1; thickening 45%									
2	−802	−910	6·5	36	3	−808	−920	6·8	38
2	−798	−892	7·0	39	Average	−800	−910	6·8	38
0·1N-Sodium borate, pH 9·2; thickening 51%									
2	−788	−900	7·2	40	Average	−790	−905	7·1	39·5
3	−796	−910	7·0	39					
0·1N-Sodium carbonate, pH 11·5; thickening 95%									
2	−775	−860	9·0	50	Average	−790	−880	9·15	51
3	−803	−904	9·3	52					
0·1N-Sodium hydroxide, pH 12·5; thickening 120%									
1	−805	−870	11·0	61	3	−820	−920	10·2	57
1	−795	−900	10·2	57	Average	−810	−900	10·5	58

DISCUSSION

Table 1, col. 2, shows that the oxide films on pickled iron were all reduced at about −0·82 v irrespective of the solution in which the specimens were inhibited; furthermore, this potential was similar to that at which the air-formed oxide film was reduced, −0·80 v, at 40 μA/cm.² (Table 1 of preceding paper); the potentials of hydrogen evolution were also the same, whether the specimens had been inhibited or not. Mild steel and reduced iron behave similarly, although sometimes the potentials of hydrogen evolution differ slightly more.

The fact that both the air-formed films and those produced by the inhibitors were reduced at the same potentials confirmed that the same material was being reduced. Further evidence that only one phase is produced during inhibition was provided by Brasher and Stove [4] who found that the benzoate content of the films produced on mild steel by sodium benzoate containing radioactive carbon was only 0·01 μg./cm.² (calc. as sodium benzoate); this value was independent of the concentration of sodium benzoate and the time of immersion. As the air-formed film on mild steel is about 37 Å thick (1·9 μg. of γ-Fe_2O_3/cm.²) and thickens by 40% (Table 2) when immersed in sodium benzoate (equivalent to an increase of 0·8 μg. of γ-Fe_2O_3/cm.²), the material formed by the inhibitor contains only about 1·0% of benzoate ions.

The results (Tables 1—3) indicate that the air-formed film on pickled iron thickened by 35—59% when immersed in the inhibiting solutions, on pickled mild steel by 18—56% and on iron reduced in hydrogen by 45—120%. The thickening increased with pH (clearly shown by the reduced specimens, but less definitely by pickled ones) and occurred almost entirely within the first 24 hr. of immersion, but there was slight indication that it continued slowly thereafter.

It was concluded that when pickled mild steel or iron or iron reduced in hydrogen was immersed in these solutions the air-formed film was rapidly thickened by 20—120% by formation of anhydrous cubic oxide of similar composition. Consequently inhibition cannot be attributed solely to adsorption, or to the repair of weak spots in the air-formed film; the question of how inhibitive solutions produce such quantities of anhydrous cubic oxide irrespective of their anions will be discussed elsewhere.

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[*Received, May 20th*, 1958.]

[4] Brasher and Stove, *Chem. and Ind.*, 1953, 558.

841. *The Cyclodehydration of Anils. Part III.* The Alternative Hydrolytic Reaction.*

By T. G. Bonner and Mary Barnard.

Anils of acetylacetone are slowly hydrolysed in aqueous sulphuric acid at acidities slightly lower than those which bring about cyclodehydration to the corresponding quinoline compound.[1] A correlation between the rate of the hydrolysis and the activities of the hydrogen ion and water in the medium has been found for 4-(2 : 3-dimethylanilino)pent-3-en-2-one which suggests a simple bimolecular mechanism.

It is concluded that cyclodehydration proceeds through the diprotonated anil, and hydrolysis through the neutral anil.

Anils of acetylacetone are very rapidly hydrolysed to the primary aromatic amine and ketone in dilute aqueous acids and use is made of this fact to stop cyclodehydration of the anil to a substituted quinoline in concentrated sulphuric acid by diluting the mixture with water.[1] At some intermediate acidity, therefore, a change occurs in the nature of the reaction between the anil and its acid environment. The two most important solvent properties affecting the point at which the transition from cyclodehydration to hydrolysis can occur are (i) the activity of protons measured by Hammett's acidity function H_0 and (ii) the activity of water, obtained from the ratio of the vapour pressure of pure water to the vapour pressure of water over the sulphuric acid–water mixture (p/p_0). The medium or range of media where the change of reaction takes place should vary with the particular anil selected since proton-accepting capacity and reactivity (whether in cyclodehydration or hydrolysis) will depend on the constitution of the anil.

Previous work on the hydrolysis of anils appears to be confined to aqueous-alcoholic solutions. It has been shown [2] that hydrolysis of 4 : 4′-disubstituted benzylideneanilines in acetate-buffered 50% aqueous methanol is a first-order reaction with respect to the benzylideneaniline. Catalysis by water or bases was negligible in comparison with acid-catalysis and at pH 3 the rate of hydrolysis became immeasurably fast. The abnormally slow acid hydrolysis of *N*-(*p*-dimethylaminobenzylidene)aniline was attributed to the formation of its less reactive conjugate acid. Another study [3] of the hydrolysis of benzylideneaniline over the pH range 6—13 indicated that below pH 11 catalysis by the hydroxyl ion was negligible, the only effective catalyst being the H_3O^+ ion; the formation of an intermediate, *N*-(α-hydroxybenzyl)aniline was postulated and evidence for it from ultraviolet and infrared absorption spectra was claimed. Measurement [4] of the rates of hydrolysis and formation of the product of condensation of a substituted benzaldehyde and *p*-toluidine has shown that practically all substituents in the *m*- and the *p*-position in the benzaldehyde portion of the anil reduce the rate of hydrolysis relatively to that of benzylidene-*p*-toluidine. This is typical of a side-chain reaction dependent mainly on the inductive effect of nuclear substituents in which either attack by an electrophilic reagent or proton addition to the side chain takes place before reaction.

Preliminary work on the anils of acetylacetone showed that hydrolysis was immeasurably rapid in 2—3N-sulphuric acid. The more acidic ranges were therefore explored for a measurable rate of hydrolysis since at the point where cyclodehydration becomes significant the hydrolysis must be relatively slow. It was found that 4-(2 : 3-dimethylanilino)pent-3-en-2-one gave a measurable rate of cyclodehydration in the range 70—81% sulphuric acid. Below 70% H_2SO_4 the cyclodehydration was too slow for measurement.

* Part II, *J.*, 1955, 2358.

[1] Bonner, Thorne, and Wilkins, *J.*, 1955, 2351.
[2] Willi and Robertson, *Canad. J. Chem.*, 1953, **31**, 363.
[3] Kastening, Holleck, and Melkonian, *Z. Electrochem.*, 1956, **60**, 130.
[4] Bloche-Claude, *Compt. rend.*, 1954, **239**, 804.

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It was shown that this anil did not remain stable in the more aqueous media below 70% sulphuric acid since when the acidity was increased considerably above this strength by rapid addition of pure sulphuric acid the yield of cyclodehydration product, 2 : 4 : 7 : 8-tetramethylquinoline was very much less than that obtained when the anil was treated directly with concentrated sulphuric acid. This result was also obtained with other anils and was fully investigated to confirm that it meant a slow hydrolysis of anil to re-form 2 : 3-dimethylaniline and acetylacetone.

Experimental

Media.—Pure sulphuric acid and sulphuric acid–water mixtures were prepared and standardised as described in Part I.[1]

Materials.—4-(2 : 3-Dimethylanilino)pent-3-en-2-one, prepared from 2 : 3-dimethylaniline and acetylacetone by the method of Turner and Roberts [5] and recrystallised twice from light petroleum (b. p. 60—80°), had m. p. 83—84°. An 89% yield of 2 : 4 : 7 : 8-tetramethylquinoline was obtained when 1 g. of this was treated with 10 ml. of concentrated sulphuric acid; [1] the m. p. of the product after crystallisation twice from light petroleum (b. p. 40—60°) was 30—31° (Found: C, 84·3; H, 8·3; N, 7·6. Calc. for $C_{13}H_{15}N$: C, 84·3; H, 8·1; N, 7·6%)

Behaviour of 4-(2 : 3-Dimethylanilino)pent-3-en-2-one in Acid.—In 2N-sulphuric acid hydrolysis to the amine and acetylacetone was virtually complete in a few minutes, colorimetric analysis of the acetylacetone by the method described in Part I indicating a 99·3% recovery. A much slower hydrolysis in 60% sulphuric acid was established by maintaining overnight at 25° a solution of 0·2 g. of anil in this medium and then adding 15 ml. of pure sulphuric acid to convert the unchanged anil very rapidly into the quinoline derivative. (It was confirmed that the cyclodehydration of this anil is immeasurably fast in the medium formed under these conditions.) 2 ml. portions of the solution were removed at hourly intervals: the acetylacetone content remained constant and corresponded to 71% hydrolysis at equilibrium. When the solution in 60% sulphuric acid was kept at 25° for 1½ hr. instead of overnight before addition of the 100% sulphuric acid, only 20% hydrolysis occurred.

Both the acetylacetone and the 2 : 3-dimethylaniline in separate solution in 60% sulphuric acid were quantitatively recoverable on dilution with water. If a mixture of these solutions, however, is kept at 25° overnight and then pure sulphuric acid added, the recovery of acetylacetone is only 74%, indicating that some anil had been formed. No product other than quinoline compound was found. In order to establish that the acetylacetone and amine form the anil only in the 60% sulphuric acid and do not condense together on addition of the pure sulphuric acid, the following experiments were carried out on a 10 ml. sample of a solution of acetylacetone in 60% sulphuric acid:

(*a*) 2 ml. of the solution were made up to 10 ml. with pure sulphuric acid; (*b*) 0·5 g. of 2 : 3-dimethylaniline was added to the remaining 8 ml. of the original solution; a 2 ml. aliquot portion was immediately removed, made up to 10 ml. with pure sulphuric acid, and kept at room temperature for 24 hr.; (*c*) the residual solution of acetylacetone and amine in 60% sulphuric acid from (*b*) was kept at room temperature for 24 hr., and a 2 ml. aliquot portion then removed and made up to 10 ml. with pure sulphuric acid. On analysis of these three solutions, 100% recovery of the acetylacetone was evident in (*a*) and (*b*) but only 67% in (*c*). The anil is therefore formed in (*c*) but not in (*b*).

Measurement of the Rate of Hydrolysis.—Kinetic measurements were carried out at 25° in a thermostat controlled within ±0·02°. The reaction vessel was a 50 ml. conical flask with a B24 neck. The anil was weighed into a B24 socket cap, the amount taken providing a 0·1M-solution when dissolved in 25 ml. of the medium. The medium was contained in a tared 25 ml. graduated flask and after being made up to the mark in the thermostat at 25° it was transferred to the reaction vessel in the thermostat. The 25 ml. flask was weighed in order to calculate the exact volume of medium used. To start the reaction, the reaction vessel was removed from the thermostat and the filled socket cap inserted. The medium and reactant were brought into contact at zero time by vigorous shaking and after complete dissolution had occurred (1—2 min.) the flask was returned to the thermostat. Six to eight 2 ml. samples were removed from the reacting mixture in the course of each experiment. Each sample was run into 7 ml. of pure

[5] Turner and Roberts, *J.*, 1927, 1832.

sulphuric acid in a 10 ml. graduated flask cooled in ice, and the solution made up to the mark at room temperature with pure sulphuric acid. This was left for 2 hr. to ensure complete conversion of unhydrolysed anil into the quinoline derivative. A 2 ml. sample was then run into 20 ml. of ice-cold water, neutralised, and made up to 50 ml. in 0·1N-sulphuric acid, and its acetylacetone content determined colorimetrically. The rate constant, k, was obtained from the kinetic equation for a reversible reaction in which a first-order hydrolysis is opposed by a second-order recombination of the products

$$kt(2a - x_e) = 2{\cdot}3x_e \log [ax_e + x(a - x_e)]/a(x_e - x)$$

where a is the initial concentration of anil, and x and x_e are the concentrations of anil at time t and at equilibrium respectively. The plot of log $[ax_e + x(a - x_e)]/a(x_e - x)$ against t was a

FIG. 1. FIG. 2.

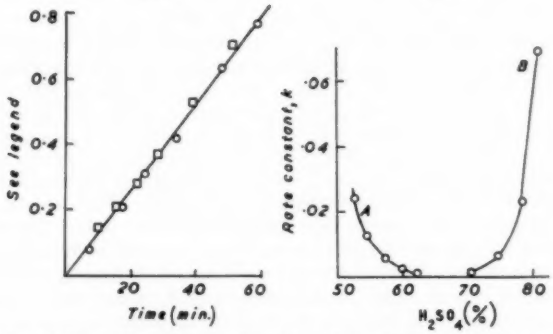

FIG. 1. *Hydrolysis of* 4-(2 : 3-*dimethylanilino*)*pent*-3-*en*-2-*one in* 52·8% H_2SO_4. $k = 0{\cdot}0241$ min.$^{-1}$. *Ordinate*: log $[ax_e + x(a - x_e)]/a(x_e - x)$.

FIG. 2. 4-(2 : 3-*Dimethylanilino*)*pent*-3-*en*-2-*one*: *A*, *hydrolysis*; *B*, *cyclodehydration*.

good straight line for all experiments. A typical duplicate result is shown in Fig. 1. Rates of hydrolysis over the range 52—62% sulphuric are given in the Table.

Rates of hydrolysis of 4-(2 : 3-*dimethylanilino*)*pent*-3-*en*-2-*one* (*initial concn.* 0·1M) *at* 25°.

H_2SO_4 (%)	10^3k (min.$^{-1}$)	log $k + H_0$	log p/p_0	log $k - H_0 -$ log p/p_0
62·4	0·962, 0·973	−7·63	−0·88	2·49
60·1	2·25, 2·27	−6·96	−0·76	2·46
57·7	5·34	−6·34	−0·66	2·46
54·9	12·7, 12·4	−5·64	−0·58	2·42
52·8	24·1, 24·1	−5·14	−0·50	2·40
60·1 *	5·33, 5·38			

* M-$(NH_4)_2SO_4$ present.

Results and Discussion

Ionisation of Anils in Sulphuric Acid.—Previous investigation [1] of the cyclodehydration of the acetylacetone anils from aniline and *p*-toluidine in the range 85—97% sulphuric acid established that the kinetic results satisfied the relation [6] log $k + H_0$ = Constant, where k is the rate constant for the cyclodehydration and H_0 the Hammett acidity function for the corresponding medium. Accordingly, it was concluded that reaction proceeded through a positively charged anil formed in fractionally small amount. The cyclodehydration of 4-(2 : 3-dimethylanilino)pent-3-en-2-one conforms with this result, since rates of

[6] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721; Hammett and Paul, *ibid.*, 1934, **56**, 830.

cyclodehydration measured over the range 70—80% sulphuric acid fitted the above equation (see Fig. 2 and following paper). It is evident however that in these strongly acid media, an anil may be almost entirely present in the monoprotonated form,[7] and in this case the result obtained would suggest that the cyclodehydration occurs in a diprotonated anil present in fractionally small amount, the bulk of the anil being present in a stable monoprotonated form. The relation deduced[1] would then be log $k + H_+ =$ Constant, where H_+ is an acidity function evaluated in the same way as H_0 but by means of bases carrying a single charge which form a doubly positively charged conjugate acid. As the H_+ acidity function had not then been evaluated, this equation could not be tested but recently[8] it has been shown that H_0 and H_+ are parallel functions of medium composition. The original result therefore satisfies both the above equations. Evidence in favour of complete monoprotonation of anils in these media was sought by determining the lowering of freezing point of a solution of an anil in pure sulphuric acid. The anil selected was 4-*p*-chloroanilinopent-3-en-2-one which was found[5] to be stable but incapable of cyclisation in the concentrated acid. A spectroscopic examination of this anil in pure sulphuric acid showed that it remained unchanged during the time taken to determine the freezing point. No special apparatus was employed for the f. p. determination and the method used[9] of comparing the *i*-factor with that of a neutral compound known to form its conjugate acid quantitatively in pure sulphuric acid was found to be adequate. The neutral compound used was benzoic acid and a satisfactory value of 2·07 was found for the *i*-factor for this solution. The *i*-factor for the depression of f. p. by the anil under the same conditions was found to be 2·05. If this result is general for anils of this type, it can be concluded that over the range of sulphuric acid media where measurable rates of cyclodehydration are found, the anil is almost entirely present as a stable monoprotonated form, the ring closure occurring through a diprotonated form. The decrease in rate of this reaction as the acidity of the medium is reduced is due to the decreasing degree of formation of this species from the monoprotonated form. Further decrease in acidity will eventually result in the appearance of the neutral anil and at that point it is likely that very little, if any, of the diprotonated species will be present. An alternative mechanism to the rate-determining ring closure which would give the same correlation of log k and H_+ is one in which a rate-determining elimination of water from the diprotonated anil is followed by rapid ring closure. There are however no theoretical grounds for assuming that the diprotonated anil would eliminate water at a measurable rate. Any species directly formed by elimination of water would be highly unstable and likely to give rise to products other than the quinoline derivative. No evidence has been found for any other product.

Mechanism of Hydrolysis of Anils.—The results in the Table show that the highest acidity at which a measurable rate of hydrolysis is obtained is about 63% sulphuric acid and that the hydrolysis becomes more rapid as the acidity of the medium is decreased by further addition of water. Ammonium sulphate is also known to decrease the acidity of sulphuric acid solutions and its addition in molar concentration to one of the media more than doubles the rate of hydrolysis. Since this salt reduces acidity without increasing the water content of the medium, its effect corresponds to altering an equilibrium in the direction of forming a large proportion of the species actually undergoing the hydrolysis. Increasing the water content of the solution could have the same effect but it is difficult to separate the extent of this effect on the rate from that due to the increasing concentration of water as a reactant in the hydrolysis. If it is assumed that the species undergoing hydrolysis is the neutral anil the marked increase in rate of hydrolysis shown in Fig. 2 would follow from the rapid change which is known to occur in the ionisation ratio $[AH^+]/[A]$ for a base A and its conjugate acid AH^+ in the appropriate range of sulphuric acid–water mixtures.

[7] Professor F. A. Long, personal communication.
[8] Bonner and Lockhart, *J.*, 1957, 364.
[9] Williams and Hardy, *J.*, 1953, 2560.

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Hydrolysis of the neutral anil by water to form the amine and acetylacetone would lead to the following kinetic analysis:

Let A and AH^+ represent the neutral anil and its conjugate acid respectively. Assuming that these are the only forms of the anil present and that $[AH^+] \ll [A]$ in the media in which measurable rates of hydrolysis are obtained, we have by the Brønsted treatment:

$$\text{Theoretical rate} = k_0K(A)(H_2O)/f_\ddagger$$

where k_0 is the theoretical rate constant, K is the equilibrium constant for the equilibrium between the reactants and the transition complex, $f_\ddagger$ is the activity coefficient of the latter, and the parentheses denote activities

$$\text{Experimental rate} = k[A]_T$$

where $[A]_T$ is the stoicheiometric concentration of anil. Equating the two rate equations we have

$$k[A]_T = k_0K[A](H_2O)f_A/f_\ddagger$$

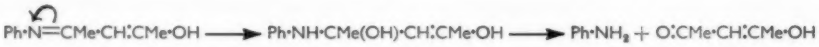
and since $[A]_T \simeq [AH^+]$

$$k[AH^+]/[A] = k_0K(H_2O)f_A/f_\ddagger$$

Taking logarithms and substituting for the term $\log [AH^+]/[A]$ from the equation $H_0 = pK_a - \log [AH^+]/[A]$, it follows that

$$\log k - H_0 - \log (H_2O) = \log k_0Kf_A/f_\ddagger - pK_a$$

which is a constant if the activity coefficient ratio $f_A/f_\ddagger$ is constant over the range of media employed. Since the two species concerned, *i.e.*, the anil and the transition complex, are both neutral this is a reasonable expectation. The above equation was tested by using the known values [6] of H_0 and of $\log (H_2O)$ (ref. 10) at 25°. The results given in the Table indicate the constancy attained and at the same time show that the simpler relation $\log k + H_0 = \text{Constant}$ is not obeyed for the hydrolysis. The reaction can be readily represented as a nucleophilic attack by water on the carbon atom of the azomethine bond as shown:



The stability of the monoprotonated anil can be attributed to the loss of resonance represented in structures (I) and (II) by any similar bonding with a water molecule.

An analogous case is provided by the abnormal behaviour on hydrolysis of *N*-(*p*-dimethylaminobenzylidene)aniline previously referred to.[2] Hydrolysis in dilute aqueous acid would require the loss of resonance energy corresponding to the two resonance structures (III) and (IV) of its stable conjugate acid, and in consequence this reaction is extremely slow.

The conjugate acid of the parent benzylideneaniline will only have one stable resonance structure, *i.e.*, that corresponding to (III), and the carbon atom of the azomethine bond will be an electron-deficient centre for attack by water, giving a much faster rate of hydrolysis, as found experimentally.

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[10] Gold and Hawes, *J.*, 1951, 2102.

842. *The Cyclodehydration of Anils. Part IV.*[1] *Substituent Effects.*

By T. G. Bonner and Mary Barnard.

Substituent effects have been studied in the cyclodehydration of substituted 4-anilinopent-3-en-2-ones to the corresponding 2 : 4-dimethylquinolines in strongly acidic aqueous media. The *m*-halogeno-derivatives all cyclise faster than the unsubstituted compound, in accord with stabilisation of the transition complex by electron-release from the halogen atom.

Additivity of substituent effects has been studied for both cyclodehydration and hydrolysis of disubstituted 4-anilinopent-3-en-2-ones and compared with the additivity of pK_a values of the anilinium ions. The enhanced interaction of the substituents in 2 : 3-disubstituted derivatives in particular is noted and discussed.

The correlation reported previously[2] between the rate constant, k, for cyclodehydration of acetylacetone anils to 2 : 4-dimethylquinolines and Hammett's acidity function, H_0, given by the equation:

$$\log k + H_0 = \text{Constant} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

was established for the anils of aniline and *p*-toluidine over the range aqueous 85—97% sulphuric acid. The ratio of the rate constants for these two anils k_{Me}/k_H is reasonably constant over the range of medium common to both compounds. This is expected since the mechanism of ring closure should be independent of the constitution of the anil. The ratio is most conveniently evaluated from the difference in the mean values of the sum, $\log k + H_0$, for the cyclodehydration of each compound over the range of media studied. This gives $k_{Me}/k_H = 6$ which is in accord with the activating effect of a methyl group *meta* to the point of electrophilic substitution in the benzene ring. A much greater activating effect with measurable rates of cyclodehydration requiring more aqueous sulphuric acids should be found for 4-*m*-toluidinopent-3-en-2-one where the methyl group is *para* to the point of ring closure. The most acid medium in which the cyclodehydration of the

Table 1. *Rates of cyclodehydration of* 4-(2 : 3-*dimethylanilino*)*pent-3-en-2-one* (*initial concn.* 0·05M) *at* 25°.

H_2SO_4 (%)	10^2k (min.$^{-1}$)	$\log k + H_0$	$\log k + C_0$	$HClO_4$ (%)	10^2k (min.$^{-1}$)	$\log k + H_0$
80·8	6·92, 6·97	−8·31	−15·54	71·4	11·1, 11·5	−9·02
78·6	2·26, 2·23	−8·31	−15·42	69·4	6·52, 6·52	−9·03
74·8	0·592, 0·586	−8·36	−15·03	66·7	1·09, 1·07	−8·92
70·5	0·135, 0·140	−8·39	−14·54	63·6	0·164, 0·164	−8·91

m-methylanilino-compound could be accurately measured was 83% sulphuric acid. The ratio k_{Me}/k_H calculated from the corresponding log k and H_0 values was then *ca.* 700. The 3 : 4- and 2 : 3-dimethylanilino-compounds similarly gave high values for this ratio (k/k_H = 1180 and 430 respectively). As the latter anil proved to be the most convenient for a study of the hydrolysis,[1] it was used also for a more extensive study of the cyclodehydration. The rate of cyclodehydration of this anil was measured in the range 70—80% aqueous sulphuric acid and also in aqueous perchloric acid. The results given in Table 1 show that equation (1) is obeyed in these more aqueous solutions and that the lack of correlation between the rate constant and the acidity function, C_0 (ref. 3) (or J_0; ref. 4), previously noted[1] is confirmed. The plot of log k against H_0 was a good straight line for both media with a slope of −1·09 for sulphuric acid and of −0·92 for perchloric acid. It can be concluded that over a considerable range of aqueous acidic media (from $H_0 = -5·5$

[1] Part III, preceding paper.
[2] Bonner, Thorne, and Wilkins, *J.*, 1955, 2351.
[3] Deno, Jaruzelski, and Schriesheim, *J. Amer. Chem. Soc.*, 1955, **77**, 3044.
[4] Gold and Hawes, *J.*, 1951, 2102.

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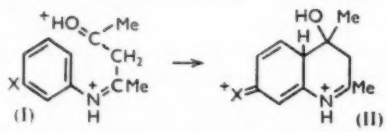
to −9·1) the cyclodehydration proceeds by a rate-determining internal electrophilic substitution of the diprotonated form of the anil which is present in fractionally small amount.[1]

Halogen Substituents.—It has been noted [5] that while 4-*m*-chloroanilinopent-3-en-2-one cyclises in concentrated sulphuric acid to 7-chloro-2 : 4-dimethylquinoline the corresponding *p*-chloro- and 3 : 5-, 2 : 5-, and 2 : 4-dichloro-anils fail to react. Since halogen deactivates the benzene nucleus to attack by electrophilic reagents, the rate of cyclo-

TABLE 2. *Rates of cyclodehydration of* m-*halogenoanils in* 93·8% *sulphuric acid at* 25°.

4-Anilinopent-3-en-2-one	*m*-F	*m*-I	*m*-Cl	*m*-Br	H
10^2k (min.$^{-1}$)	4·16	1·90	0·83	0·696	0·371

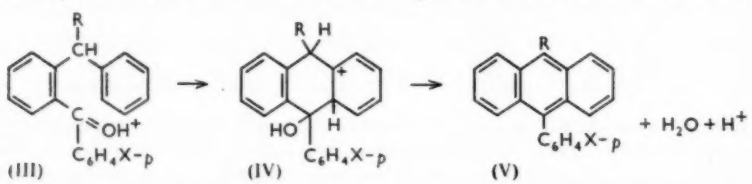
dehydration for the *m*-chloroanil should be less than for the unsubstituted anil. However, this was not found to be the case, as the results in Table 2 show. The experimental result for 4-anilinopent-3-en-2-one is halved to allow for the fact that there are two identical points of ring closure in this compound compared with one only in its *meta*-substituted derivatives. In all four *m*-halogenoanils, the halogen atom activates the *para*-position relative to hydrogen, the order being F > I > Cl > Br > H. Activation is readily explicable in terms of the stabilisation of the transition complex by operation of the electromeric effect of halogen. The diprotonated side chain in the anil (I) can transfer one



(I) (II)

of its positive charges to the halogen atom, X, in forming the intermediate (II) which must resemble closely the transition state in the reaction. The quinoline produced results from loss of a molecule of water and a proton from this intermediate. The inhibitory inductive effect is clearly still operative since the rate of cyclodehydration of the corresponding *m*-toluidine anil is several hundred times greater still. The inductive effect, however, is secondary to the polarisability of the halogen atoms under the influence of the strong electrical field in the cyclic transition state.

Another cyclisation in which the effect of halogen has been studied is the conversion of



(III) (IV) (V)

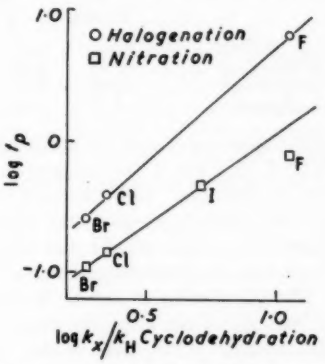
2-benzyl-4′-halogenobenzophenones to 9-*p*-halogenophenylanthracenes (V) in hydrobromic–acetic acid.[6] Here the rate of cyclisation is hardly affected by *p*-halogeno- (or even *p*-methyl) substituents and this is in accord with the formation of a transition state in which the electromeric effect cannot operate, as shown in (III) and (IV).

The similarity in operation of the polarisability effect of halogens in other electrophilic substituents is shown by a comparison of the rates of cyclodehydration with the partial rate factors for *para*-substitution in nitration and halogenation of the corresponding halogenobenzenes.[7] As shown in the Figure a linear relation exists between log *k* (cyclodehydration) and log f_P in both cases, the sole exception being the fluorine substituent in

[5] Turner and Roberts, *J.*, 1927, 1836.
[6] Bradsher and Vingiello, *J. Amer. Chem. Soc.*, 1949, **71**, 1434.
[7] de la Mare, *J.*, 1954, 4450.

nitration. This is further evidence for the efficacy of the nitronium ion as an electrophilic reagent, since it does not evoke the full operation of the polarisability of the fluorine atom. The view that halogenation by means of the less effective halogen molecule is more powerfully electron-demanding [8] clearly applies to the cyclodehydration.

A recent example of activation by a *p*-fluorine substituent has been found in the solvolysis of halogenobenzyl toluene-*p*-sulphonates in aqueous acetone.[9] The sequence of decreasing rate constants, *p*-F > H > *p*-Cl > *p*-I > *p*-Br, demonstrates the superior conjugating effect of fluorine in stabilising the transition state in this reaction, but it is evident that for the other halogens the balance of conjugative and inductive effects is not identical with that of the cyclodehydration. In the correlation found between the rate constants of the solvolysis and of nitration of the corresponding halogenobenzenes, only the *p*-fluoro-substituent showed a considerable deviation. It was suggested that this was due to the decreased availability of the non-bonding electrons of the fluorine atom in the nitration by hydrogen-bonding with the highly acidic medium. The similar deviation



Comparison of rates of halogenation, nitration, and cyclodehydration at the para*-position to halogen.*

evident in the correlation of the rates of cyclodehydration and nitration shown in the Figure does not support this proposal since in this case the medium is the same for both reactions.

The complete failure of 4-*p*-chloroanilinopent-3-en-2-one to cyclise was confirmed and it is evident that in this compound and the dichloroanils referred to above the deactivating inductive effect of halogen *meta* to the point of ring closure predominates.

Additivity of Substituted Effects.—Before considering the effects of substituents in the cyclodehydration of disubstituted anils, it is convenient to review the additivity of these effects in the acid dissociation constants of the corresponding anilinium ions. Substituent effects will be additive if the experimental value for $pK_a^{X,Y}$ fits equation (2):

$$pK_a^{X,Y} = pK_a^{X} + pK_a^{Y} - pK_a^{H} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Previous results [10,11] show that the biggest deviation from additivity occurs with 2 : 6-xylidine where the lower pK_a value indicates that the amine is less basic than if the effects of the two methyl groups were strictly additive. In contrast, the 2 : 3-xylidine is a stronger base than expected. Steric hindrance of resonance in the base is frequently invoked to account for the increased basicity of an aromatic amine when bulky substituents such as methyl are introduced in the *ortho*-positions [12] but the lower basicity of *o*-toluidine compared with aniline and the *m*- and *p*-toluidines is in contradiction to the operation of

[8] de la Mare and Waters, *Ann. Reports*, 1953, **50**, 127.
[9] Fang, Kochi, and Hammond, *J. Amer. Chem. Soc.*, 1958, **80**, 563.
[10] Beale, *J.*, 1954, 4495.
[11] Gillois and Rumpf, *Bull. Soc. chim. France*, 1954, **21**, 112.
[12] Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827; Wheland, "Resonance in Organic Chemistry," Chapman and Hall Ltd., London, 1955, p. 372.

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this factor; in this case, the difference has been attributed to a sterically hindered solvation of the *o*-toluidinium ion.[13] The latter effect would account for the decreased basicity of 2 : 6-xylidine and the former for the increase in 2 : 3-xylidine but it is difficult to predict which of the two effects would predominate in any given compound. Similar differences in behaviour have also been observed between 2 : 5- and 2 : 3-dimethyl derivatives of benzene of the type XYC_6H_3R where R = NO_2[14] or CO_2H,[15] in that the introduction of the 3-methyl but not the 5-methyl substituent increases the influence of the 2-methyl substituent on the interaction between the group R and the benzene ring. For the remaining compounds in Table 3 it is evident that the substituent effects are reasonably additive.

The test of additivity in the cyclodehydration reaction is obtained by replacing the pK_a terms in equation (2) by the logarithms of the rate constants of cyclodehydration and assuming that the value of the acid dissociation constant of the diprotonated anilinoanil AH_2^{++} is not greatly affected by nuclear substituents. The results in Table 4 show that an additivity of substituent effects in the cyclodehydration is found only for the 2 : 4-di-

TABLE 3. pK_a *values of disubstituted anilines.*

Aniline	Found	Calc.	Diff.	Aniline	Found	Calc.	Diff.
2 : 6-Dimethyl	3·95	4·26	−0·31	3 : 4-Dimethyl	5·17	5·23	−0·06
2 : 3-Dimethyl	4·70	4·57	+0·13	2 : 5-Dimethyl	4·53	4·57	−0·04
2 : 4-Dimethyl	4·89	4·91	−0·02	5-Chloro-4-methyl ...	4·05	4·09	−0·04

methylanilino-anil and the 3-chloro-4-methylanilino-anil. The largest deviations occur in the 2 : 3- and the 3 : 4-dimethyl compound, and are in the direction of greatly decreased rates of reaction. In both cases this effect can be interpreted as steric inhibition by the adjacent methyl group of the full operation of the electromeric effect of the 3-methyl substituent. This would reduced to some degree the stabilisation of the transition complex by the resonance structure corresponding to (II).

The peculiarity of the 2 : 3-disubstituted anils is analogous to the unusual effect on the basicity of the adjacent methyl groups in 2 : 3-xylidine, to which reference has been made above. This effect is also evident in the hydrolysis of the anils. The hydrolysis

TABLE 4. *Additivity of substituent effects.*

			Cyclohydration			
4-Anilinopent-2-en-2-one	log k^X	log k^Y	log k^H	Calc.	log $k^{X,Y}$ Found	Diff.
2 : 3-Dimethyl	−1·99	0·41	−2·43	0·85	0·20	−0·65
2 : 4-Dimethyl	−1·99	−1·58	−2·43	−1·14	−1·14	0
3 : 4-Dimethyl	0·41	−1·58	−2·43	1·26	0·64	−0·62
3-Chloro-4-methyl	−2·08	−1·58	−2·43	−1·23	−1·27	−0·04
3-Chloro-2-methyl	−1·99	−2·08	−2·43	−1·64	−2·00	−0·36
			Hydrolysis			
4-Anilinopent-3-en-2-one	log k^X	log k^Y	log k^H	Calc.	log $k^{X,Y}$ Found	Diff.
2 : 3-Dimethyl	−2·17	−1·56	−1·34	−2·39	−2·65	−0·26
2 : 4-Dimethyl	−2·17	−1·74	−1·34	−2·57	−2·57	0
3 : 4-Dimethyl	−1·56	−1·74	−1·34	−1·96	−1·90	+0·06

Rates of cyclodehydration were determined in 93·8% sulphuric acid at 25°, except those of the *m*-methyl, 2 : 3-dimethyl, and 3 : 4-dimethyl compounds. The last three were measured in 74·8% sulphuric acid and the values in the 93·8% acid calculated from equation (1). All rates of hydrolysis were determined in 60·1% sulphuric acid at 25°.

rates given in Table 4 show that while the effects of methyl groups in the 2- and the 4-position are additive, the rate of hydrolysis of the 2 : 3-dimethylanilino-compound is less than expected. It has been suggested that the enhanced effect of the 2-methyl substituent on an adjacent side chain due to the repulsion of a 3-methyl substituent operates by reducing the coplanarity of the side chain with the benzene ring.[15] This

[13] Brown and Cahn, *J. Amer. Chem. Soc.*, 1950, **72**, 2939.
[14] van Helden, Verkade, and Wepster, *Rec. Trav. chim.*, 1954, **73**, 39.
[15] Dippy, Hughes, and Laxton, *J.*, 1954, 1470.

would clearly result in the increased basicity of 2 : 3-xylidine. The slower hydrolysis of the 2 : 3-dimethylanilino-compound found experimentally would also be expected since the greater electron-density in the neighbourhood of the azomethine bond would hamper the nucleophilic attack by water. The reduced rate of cyclodehydration of 4-(2-chloro-3-methylanilino)pent-3-en-2-one has a similar explanation if it is assumed that there is an increase in the repulsion between the chlorine and the methyl substituent due to the side chain which decreases the conjugation of the 3-methyl group with the ring and reduces the contribution of the resonance structure corresponding to (II).

In the hydrolysis methyl groups in all positions reduce the rate, in contrast to their activating effect in cyclodehydration, and this is in accord with the mechanism proposed in the preceding paper of nucleophilic attack by water on the carbon atom of the side chain adjacent to the nitrogen atom. As might be expected in a side-chain reaction, the results for the hydrolysis of both the monosubstituted and the disubstituted anils (except the 2 : 3-dimethylanil) fit the Hammett equation: [16]

$$\log k/k_0 = \rho\sigma$$

where k and k_0 are the rate constants for the substituted and unsubstituted anils respectively, ρ is a constant characteristic of the reaction, and σ a constant characteristic of the substituent. The plot of log k/k_0 against Hammett's original σ values is a straight line and the value of ρ from the slope is 1·91. The fact that ρ is positive indicates a reaction facilitated by a low electron-density at the reaction site. No similar correlation of rate constant with the σ values recently proposed [17] for electrophilic aromatic substitution was found for the cyclodehydration.

TABLE 5. *Activation energies* (± *ca.* 300 *cal.*) *in cyclodehydration.*

	4-*p*-Toluidinopent-3-en-2-one		4-Anilinopent-3-en-2-one	
H_2SO_4 (%)	E_A (cal.)	$\log_{10} A$	E_A (cal.)	$\log_{10} A$
94·9	15,900	10·4	17,400	10·9
91·2	16,500	10·4	15,600	9·1
86·8	17,300	10·5	—	—

Constants of the Arrhenius Equation.—Rates of cyclodehydration of both anilino- and *p*-toluidino-anils were measured over the range 0—50° in different media to evaluate the constants, A and E, of the equation $\log k = \log A - E/RT$ which are given in Table 5. Reproducible results could not be obtained for the anilinoanil in 86·8% sulphuric acid, possibly because of some hydrolysis in this medium.

EXPERIMENTAL

Media.—Pure sulphuric acid and sulphuric acid–water mixtures were prepared and standardised as described in Part I.[2] Perchloric acid–water mixtures were prepared from "AnalaR" perchloric acid and similarly standardised.

Materials.—Acetylacetone was dried over potassium carbonate and distilled. The majority of aromatic amines were obtained from B.D.H. or Light and Co. and were recrystallised or distilled under reduced pressure. *m*-Iodoaniline was obtained by reduction of *m*-nitroaniline. 3-Chloro-4-methylaniline was prepared from 2-methyl-5-nitroaniline by diazotisation and treatment with cuprous chloride.[18] 4-Chloro-3-methylaniline was obtained by the action of sodium chlorate and concentrated hydrochloric acid on aceto-*m*-toluidide.[19]

The anils were prepared by boiling under gentle reflux a 1 : 1·1 mixture [5] of the aromatic amine and acetylacetone. Most anils were obtained in 60—70% yield by this method and were crystallised from light petroleum (b. p. 40—60°). The following substituted 4-anilinopent-2-en-4-ones do not appear to have been described previously: *m*-fluoro-, m. p. 35—36°; *p*-fluoro-,

[16] Hammett, *Chem. Rev.*, 1935, **17**, 125; Taft, "Steric Effects in Organic Chemistry," ed. by Newman, Chapman and Hall Ltd., London, 1956, p. 556; Brown and McDaniel, *J. Org. Chem.*, 1958, **23**, 420.

[17] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1957, **79**, 1913.

[18] Witt, *Ber.*, 1892, **25**, 86.

[19] Reverdin and Crépieux, *Ber.*, 1900, **33**, 2503.

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m. p. 44°; *m*-bromo-, m. p. 37—38°; *m*-iodo-, m. p. 56—57°; 2 : 4-dimethyl-, m. p. 38—40°; 3 : 4-dimethyl-, b. p. 190°/20 mm.; 3-*chloro*-4-*methyl*-, m. p. 67—68·5° (Found: N, 6·5; Cl, 16·1. $C_{12}H_{14}ONCl$ requires N, 6·3; Cl, 15·9%); 4-*chloro*-3-*methyl*-, m. p. 46—47° (Found: N, 6·5; Cl, 15·6. $C_{12}H_{14}ONCl$ requires N, 6·3; Cl, 15·9%); 3-chloro-2-methyl-, m. p. 81—82°.

The corresponding quinoline compounds were obtained from these anils in 89—99% yields by dissolving 1 g. of the anil in 10 ml. of 98% sulphuric acid and keeping the solution at room temperature for several hours before isolating the product.[2] The following substituted quinolines do not appear to have been reported previously: 7-fluoro-2 : 4-dimethyl-, m. p. 45—46°; 7-bromo-2 : 4-dimethyl-, m. p. 46—47°; 7-iodo-2 : 4-dimethyl-, m. p. 54—55°; 2 : 4 : 6 : 7-*tetramethyl*-, m. p. 79—80° (Found: C, 84·4; H, 8·1; N, 7·7. $C_{13}H_{15}N$ requires C, 84·3; H, 7·9; N, 7·6%); 7-*chloro*-2 : 4 : 6-*trimethyl*-, m. p. 81—82° (Found: N, 7·1; Cl, 17·3. $C_{12}H_{12}NCl$ requires N, 6·8; Cl, 17·2%); 5-chloro-2 : 4 : 8-trimethyl-, m. p. 54—55°; 6-chloro-2 : 4 : 7-trimethyl-, m. p. 89—90°; 7-*chloro*-2 : 4 : 8-*trimethyl*-, m. p. 68—69° (Found: N, 6·8; Cl, 17·9. $C_{12}H_{12}NCl$ requires N, 6·8; Cl, 17·2%).

Measurement of Reaction Rates.—Rates of cyclodehydration in sulphuric acid–water and perchloric acid–water were determined as described in Part I.[2] It was established that neither sodium perchlorate nor any of the amines or quinoline compounds investigated interfered with analysis of the mixtures, in which the acetylacetone obtained from unchanged anil is converted into its ferric salt which is determined colorimetrically. A small refinement was introduced to obtain the reference curve for standard solutions of acetylacetone prepared from the pure ketone. Two reference curves were obtained, the prepared solutions for analysis in one case containing 1·62 g. of sodium sulphate per 40 ml., and in the other case 3·24 g. of sodium sulphate per 40 ml. These are the lower and the upper limit of sodium sulphate concentrations in the solutions obtained for colorimetric analysis from reaction mixtures. While the difference in slopes of the straight lines obtained by plotting the logarithms of the optical density ratio against concentration of acetylacetone was almost negligible, the gradients in both cases were about 3% less than the slope of the reference curve obtained in the absence of added sodium sulphate. The new reference curves were therefore preferred for the evaluation of the experimental results.

Rates of hydrolysis were determined as described in the preceding paper.[2]

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843. *Stereochemistry of Metals of the B Sub-groups. Part I. Ions with Filled* d*-Electron Shells.*

By L. E. ORGEL.

The tendency of Hg^{++}, Au^{+}, Ag^{+}, and Cu^{+} to form compounds in which the metal is attached to only two ligands is attributed to *d*–*s* mixing rather than to the special stability of *sp*-hybrid bonds.

SIMPLE theories of the structures of ionic crystals which treat the component ions as charged, non-polarisable spheres almost inevitably conclude that the most stable arrangements of anions about a given cation has high symmetry.[1] In particular, regular tetrahedral and octahedral environments are predicted to be most stable for tetra- and hexa-co-ordinated cations respectively. These are the most common arrangements encountered in inorganic stereochemistry.

The case of octaco-ordination is more complicated, for the commonly occurring arrangement of anions at the vertices of a cube is predicted to be unstable relative to their disposition at the vertices of a square antiprism, at least for an isolated XY_8 group. Presumably it is the difficulty of combining these antiprisms into a structure extended in space that prevents their common occurrence in binary compounds. The TaF_8^{3-} ion does have the square-antiprism structure and, although it has been suggested that d^4sp^3

[1] Wells, "Structural Inorganic Chemistry," 2nd edn., Oxford Univ. Press, 1950.

bonding is involved,[2] there is no reason to suppose that the observed stereochemistry is a consequence of anything other than the electrostatic repulsion between fluoride ions.

There are at least four large groups of related compounds which contain metal ions in environments of less than cubic symmetry. We have dealt with transition-metal compounds[3a] containing ions such as Cu^{++}, Cr^{++}, and Ni^{++} and with the oxides of the A subgroup such as MoO_3 and $BaTiO_3$.[3b] In this and another paper[4] we investigate a different group of ions, those either with a filled d^{10} shell or with an inert pair of s electrons. The instability of the octahedral and cubic environments for these ions in certain of their compounds is due to the energies and electronic configurations of their lowest excited states.

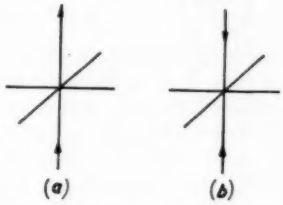
General Theory.—A similar environment might be expected for d^{10} ions and A subgroup closed-shell ions in analogous compounds. There is indeed as close a resemblance between the stereochemistry, for example of the Zn^{++} and the Mg^{++} ions as can be expected in view of their different sizes. However, ions such as Au^{+} and Hg^{++} strongly tend to form compounds of low co-ordination number, particularly linear XY_2 complexes.

Jørgensen pointed out that the tendency of d^{10} ions to form linear complexes is strongly correlated with the energies of the excited states of the configurations $(n-1)d^9ns$ and $(n-1)d^9np$ above the $(n-1)d^{10}$ ground state.[5] In Table 1 we reproduce Jørgensen's

FIG. 1.

(*a*) One component of an antisymmetric T_{1u} vibration.

(*b*) A symmetrical displacement which can mix d and s orbitals. (This is not the component of a normal mode.)



data for a number of d^{10} ions. Clearly the Au^{+}, Hg^{++}, and Cu^{+} ions which have the greatest tendency to form linear complexes are those with the lowest d^9s excited states. It has been suggested that the stability of the linear configuration for these ions is due to the formation of covalent sp bonds between the metal ions and the two ligands. We now re-examine and modify this point of view.

Consider the stability of a d^{10} cation at the centre of a regular octahedron of negative ions. An antisymmetric displacement of two or more anions as shown in Fig. 1*a* removes the centre of symmetry of the environment of the cation and so produces an electric field which can mix together d and p orbitals but not d and s orbitals. The electron configuration is thus changed from d^{10} to $d^{10-\delta}p^{\delta}$. But a symmetric displacement of anions as shown in Fig. 1*b* can mix together d and s orbitals but not d and p orbitals to give a configuration $d^{10-\delta}s^{\delta}$. If the stabilisation due to mixing brought about by either class of distortion is sufficiently large it will more than compensate for the energy lost in distorting the otherwise electrostatically stable regular octahedron and so lead to instability. Since it is the d–s rather than d–p separation that is exceptionally small for certain d^{10} ions we should expect symmetric distortions to be more important. We now make plausible that for any assumed regular octahedral complex there must be a range of d–s (or d–p) separations which lead to instability.

The d_{z^2} and s orbitals shown in Fig. 2*a* can be mixed together (hybridised) to give two new orbitals as shown in Fig. 2*b*. If the two electrons which occupy the d_{z^2} orbital

[2] See Gillespie and Nyholm, "Progress in Stereochemistry," Butterworths, London, 1958, Vol. 2, for references.

[3] (*a*) Dunitz and Orgel, *J. Phys. Chem. Solids*, 1957, **3**, 20, and references therein; (*b*) Orgel, *Discuss. Faraday Soc.*, 1958, in the press.

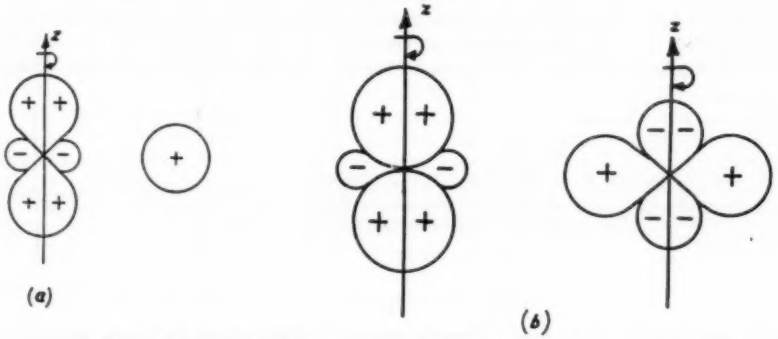
[4] Orgel, unpublished work.

[5] Jørgensen, Thesis, Copenhagen, 1957.

of the free ion are put into the $(1/\sqrt{2})(d_{z^2} + s)$ orbital the atom develops a strong electronegativity in the x- and y-directions, while if the $(1/\sqrt{2})(d_{z^2} - s)$ orbital is occupied the opposite is true. If the d_{z^2} and s orbitals are initially degenerate the stable configuration of the octahedron must necessarily be distorted, since d–s mixing can occur without expenditure of energy in the regular octahedral configuration and, in view of the strongly directional electronegativity of the atom, a subsequent distortion of the octahedron must lead to stabilisation. If the d and s orbitals are not degenerate then the expenditure of energy required to produce d–s mixing is proportional to the d–s separation, and so it is mainly this quantity which determines whether the regular octahedral configuration is stable or not. Clearly for any given octahedral environment there must be a range of d–s separations which lead to instability.*

Structural Evidence.—The structural evidence of ions with filled d shells shows that the Zn^{++} and Cd^{++} ions occur in normal tetrahedral or octahedral environments. On the

FIG. 2.



(*a*) The d_{z^2} and s orbitals.
(*b*) Hybrid orbitals concentrated along the z axis and in the x–y plane.

other hand the Au^{+} and Hg^{++} ions are frequently encountered as discrete XY_2 groups, or in environments based on octahedral co-ordination but strongly distorted in such a way as to maintain a centre of symmetry.

Typical distorted octahedral environments occur in HgS (distorted NaCl structure [1]), in a variety of halides,[1] in ammines,[1] and in $Hg(pyridine)_2Cl_2$.[8] Linear co-ordination is found for $[Ag(CN)_2]^-$ and $[Au(CN)_2]^-$ and in Cu_2O and Ag_2O.[1] In HgO there are two short collinear Hg–O bonds and two much weaker bonds at right angles.[9] Studies of complexes in solution also indicate that twofold co-ordinated complexes are particularly stable, for example, $AgCl_2^-$,[10] $Hg(OH)_2$, and $In(OH)_2^+$.[11]

Nature of the Bonding.—We attribute the differences in the stereochemistry of Zn^{++} and Cd^{++} on the one hand and Cu^{+}, Ag^{+}, Au^{+}, Hg^{++}, and perhaps Tl^{+++} on the other to the

* These arguments can be made precise along lines very similar to those used in treatments of the Jahn–Teller distortions.[6,7] It then appears that the stabilisation of the distorted octahedral environment by d–s mixing is determined by the ratio of the matrix element between the s and d orbitals of the potential produced by a distortion of the environment to the d–s separation. This stabilisation can be expanded in powers of the displacement along the normal co-ordinate corresponding to the E_g stretching vibration. If the quadratic term in this expansion exceeds the restoring term due to other interactions the octahedral configuration is unstable. The existence of a range of d–s separations for which the regular octahedral environment is unstable can thus be established.

[6] Jahn and Teller, *Proc. Roy. Soc.*, 1937, *A*, **161**, 220.
[7] Longuet-Higgins, Öpik, Pryce, and Sack, *Proc. Roy. Soc.*, 1958, *A*, **244**, 1, and references therein.
[8] Grdenić and Krstanović, *Archiv Kem.*, 1955, **27**, 143.
[9] Aurivillius, *Acta Chem. Scand.*, 1956, **10**, 852.
[10] Stability Constants, Part II, Chemical Society Special Publication No. 7, 1958.
[11] Basolo and Pearson, "The Kinetics of Inorganic Reactions," Wiley, New York, 1958.

much smaller *d*–*s* separations in the latter group. Only for these ions can the stabilisation due to *d*–*s* mixing compensate for the loss of energy which normally results from a small co-ordination number.

Although a purely electrostatic account of these ions has been given, covalent bonding must clearly be important in such compounds as $Hg(CH_3)_2$ or $Tl(CH_3)_2^+$ and also in $HgCl_2$, $HgBr_2$, etc. To account for the correlations between the stability of these linear compounds and the *d*–*s* separation we must, in a covalent-bonding theory, suppose that instead of forming *sp* hybrids the central ion uses one *p* orbital and one *d*–*s* orbital. The extra stability of linear compounds of Hg^{++}, etc., is largely due to *d*–*s* mixing although we do not exclude the possibility that *sp* hybridisation of the kind normally postulated occurs here as in other linear triatomic molecules.

TABLE 1. *Energies (cm.*$^{-1}$*) of lowest* d^9s *and* d^9p *states above the* d^{10} *ground state.*

	Cu^+	Zn^{++}	Ag^+	Cd^{++}	Au^+	Hg^{++}	Tl^{+++}
$nd^9(n+1)s$	21,928	78,105	39,164	80,463	15,039	42,862	75,052
$nd^9(n+1)p$	66,418	137,876	80,173	139,042	63,052	118,616	147,635

TABLE 2. *Ionisation potentials and* s–p *separations of* Zn, Cd, *and* Hg.

	1st I.P. (ev)	2nd I.P. (ev)	$E(s-p)$ of M^+ (cm.$^{-1}$)
Zn	9·39	18·0	49,000
Cd	8·99	16·9	45,800
Hg	10·44	18·8	57,600

Since this view differs from that usually expressed, we shall consider the alternative hypothesis of *sp* hybridisation in more detail. The greater stability of the *s*-orbital in Hg than in, say, Zn is seen clearly from Tables 1 and 2 which show that the sum of the first two ionisation potentials of Hg is almost 2 ev greater than the corresponding sum for Zn. However this alone, while it would account for a greater stability of Hg^{++} than of Zn^{++} compounds, does not account for the unusual stereochemistry of the Hg^{++} ion. To understand the latter we must look at the 6*s*–6*p* separation rather than at the absolute energies of the *s* orbitals, for it is that separation which determines the relative stabilities of *sp* and sp^3 hybrids. Now the *s*–*p* separation is about 1 ev greater in Hg than in Zn and in Hg^+ than in Zn^+. While this could certainly influence the stereochemistry it hardly seems large enough compared with the total energy of the *s* and *p* orbitals to account for the great differences between the two elements. The *d*–*s* separation on the other hand is almost halved between Zn^{++} and Hg^{++} and this is more likely to have a drastic influence on the co-ordination.

While we have been able to rationalise the stereochemistry of Hg^{++} compounds, etc., in terms of a simple theory we must point out that this theory is not predictive in one sense—it is not possible to say *a priori* whether an arrangement with two electrons in the $(1/\sqrt{2})(d-s)$ orbital and two short bonds or with the electrons in the $(1/\sqrt{2})(d+s)$ orbital and four short bonds is more stable. Experimentally two bonds always seem to be shorter in compounds containing the Hg^{++} ion, presumably because of some preference for *sp*-hybrid bond formation.

Conclusions.—We have discussed the d^{10} ions in some detail in order to emphasise points of interest to the more important problem of the stereochemistry of ions with inert pairs. (1) Ionic crystals of high symmetry are likely to be unstable to those distortions which mix together filled and unfilled orbitals of similar energy. (2) The distortions can be understood in terms of electrostatic interactions, but this does not disprove the occurrence of a measure of covalent bonding. Distortions from cubic symmetry are not diagnostic of bond type. (3) While simple theoretical arguments define the symmetry class of displacements which stabilise d^{10} ions, they do not pick out one unique distortion, for the displacements invariably correspond to degenerate vibrations. The actual co-ordination in any particular compound is determined in part by the finer details of the forces between the ions within a complex and in part by packing considerations in the

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crystal. (4) The extent of the distortion can have any magnitude from a relatively small one to one which effectively removes some ions from the co-ordination group. In extremely distorted environments it may be better to consider the resulting structure in its own right rather than as derived from a more symmetric structure.

The *d*–*s* mixing postulated is capable of experimental investigation by nuclear magnetic and quadrupole resonance experiments. We have shown [12] that interconfigurational mixing leads to paramagnetic terms in the chemical screening constants for d^{10} and $d^{10}s^2$ ions and that *sp* mixing accounts for the observed chemical shifts in Pb^{++} compounds. Comparable studies on d^{10} ions should enable the extent of *d*–*s* mixing to be estimated.

Mixing of *d* and *s* orbitals in tetrahedrally co-ordinated compounds by distortion of the regular cubic environment is also to be expected. The phase transitions in and a number of unusual features of the *X*-ray scattering from the halides of Cu^+ and Ag^+ will be discussed elsewhere.

I an indebted to Dr. C. K. Jørgensen for helpful discussions.

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CAMBRIDGE UNIVERSITY. [*Received, July 14th*, 1958.]

[12] Orgel, *Mol. Physics*, 1958, in the press.

NOTES.

844. *A Convenient Solid for Calibration of the Gouy Magnetic Susceptibility Apparatus.*

By B. N. FIGGIS and R. S. NYHOLM.

THE measurement of magnetic susceptibilities by the Gouy method is a relative one, the apparatus being calibrated in terms of a substance of known susceptibility, for which water, nickel chloride solution, and powdered cupric sulphate pentahydrate or ferrous ammonium sulphate hexahydrate have been used. The low suceptibility of water is often inconvenient if small tubes are being calibrated. Nickel chloride solution requires accurate analysis before use and ferrous ammonium sulphate is often of questionable purity. This substance and copper sulphate do not pack well and several different values for the susceptibilities of both solids have been reported.

The required properties for a calibrant are: (1) Readily available pure; (2) an accurately known and moderate susceptibility ($\chi_g \approx 10^{-5}$); (3) stability in moist air; (4) χ_g must vary in a known and simple way, at least at room temperature; (5) easily and reproducibly packable into the Gouy tube. The complex mercury tetrathiocyanatocobaltate $HgCo(CNS)_4$ offers some advantages and its susceptibility has therefore been accurately determined.

Pure water [absolute susceptibility taken as 0·7199 ($\pm$0·01%) $\times 10^{-6}$ at 20°] [2] being used as reference, the gram susceptibility of the complex is 16·44 ($\pm$0·08) $\times 10^{-6}$ at 20°. As reported elsewhere,[1] it obeys the Curie–Weiss law, $\chi_g \propto (T + 10)^{-1}$ where T is expressed in degrees absolute. Three different samples were prepared and measurements made on specimen lengths of 8, 10, and 12 cm. The following mean measurements of $10^6\chi_g$ were made: preparation no. 1, 16·45 ($\pm$0·2%); no. 2, 16·40 ($\pm$0·2%); no. 3, 16·48 ($\pm$0·3%); measurements at 8 cm., 16·38 ($\pm$0·2%); at 10 cm., 16·44 ($\pm$0·4%); at 12 cm., 16·49 ($\pm$0·4%).

It is concluded that within the experimental error of 0·4% there is no difference between

[1] Figgis and Nyholm, to be published.
[2] Piccard and Devaud, *Arch. Sci. Phys. Nat.*, 1920, **2**, 455.

the preparations or the uniformity of packing at the three lengths. Allowing for possible systematic error of 0·1% arising from uncertainty in the correction for air dissolved in, or displaced by, the water calibrant, we conclude that the susceptibility of $CoHg(CNS)_4$ is 16·44 ($\pm$0·08) $\times$ 10^{-6} and that it is a very convenient substance for standardising Gouy tubes.

Experimental

The Gouy tube consisted of a 30 cm. piece of " Pyrex " glass tube of 1·2 cm. ($\pm$0·01 mm.) bore, cut into halves and cemented together with a flat glass plate between the halves. The tube hung from the pan of an aperiodic semimicro-balance so that the separating plate was in the centre of the pole gap of an electromagnet (10-cm. pole diameter, 4-cm. inter-pole gap). The force on the Gouy tube alone was then $-0{\cdot}14$ mg. The Gouy tube was surrounded by a water jacket; the temperature was constant for long periods but varied from day to day between 19·5° and 20·5°. The temperature near to the specimen was measured frequently by means of a thermocouple; a correction was made according to $d\chi_g/dT = 0{\cdot}012\%$ for water [4] and 0·33% for $HgCo(SCN)_4$ at 20°.

An electromagnet of the Bates–Lloyd Evans [5] type was used, the current (10·0 A) being reproducible to within 0·1%. The magnetic field was approximately 10,000 gauss and since the magnet was approaching saturation field reproducibility was better than 0·1%; heating of the coils and core was kept to a minimum. By using a rider with the semimicro-balance, the beam deflection was kept within 0·5 mg. of the centre and this corresponded with a change in specimen position of approx. 0·5 mm. No deviation from linearity was noticed even when considerably larger beam deflections were allowed. The force developed on the water specimen varied from 23 to 24·5 mg. and that on the complex from 0·75 to 0·8 g.

The Gouy tube was calibrated at 8, 10, and 12 cm. marks with conductivity water which had come to equilibrium with the atmosphere. An allowance for dissolved air was made, based on its solubility in water, its partial pressure, and the value $\chi_g = 108 \times 10^{-6}$ at 20° for oxygen.[3] The calibration was also performed in nitrogen; the two calibrations agreed within experimental error, but the fluctuations introduced into the measurement of the force on the specimen by the provision of the nitrogen atmosphere were greater (0·2%) than the uncertainty introduced by the corrections for dissolved oxygen (0·1%). The volume of the meniscus was determined and allowed for. The mercury tetrathiocyanatocobaltate was introduced into the tube in lots of 1—2 g., *i.e.*, 5—10% of the total weight, and the bottom of the tube tapped firmly on wood 100 times after each addition. Three separate preparations of the substance were made and the tube was packed with each to each mark three times, a total of 27 measurements. The measurement of the force developed on each specimen was the mean of 9 observations.

The following preparation gives the complex in uniform and suitable crystal size with excellent packing properties. A solution " AnalaR " cobalt sulphate heptahydrate (28 g.) and " AnalaR " ammonium thiocyanate (30 g.) in distilled water (50 ml.) was added, at the boiling point and in one lot, to a boiling filtered solution of " AnalaR " mercuric chloride (27 g.) in distilled water (300 ml.), with vigorous stirring. The precipitated crystals are of about 0·5 mm. size. Boiling is continued for 1—2 min. with vigorous stirring. The product is washed several times by decantation and then dried at 120° (yield, 15 g.) (Found: C, 9·9; N, 11·35; S, 26·1. Calc. for $HgCo(SCN)_4$: C, 9·8; N, 11·4; S, 26·0%). The infrared spectrum of a sample stored under atmospheric conditions for a long time showed no significant water content.

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[*Received, April 29th*, 1958.]

[3] Bauer and Piccard, *J. Physique*, 1920, **1**, 97.
[4] Auer, *Ann. Physik*, 1933, **8**, 593.
[5] Bates and Lloyd-Evans, *Proc. Phys. Soc.*, 1933, **45**, *A*, 425.

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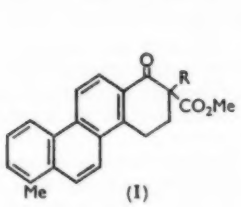
845. *Polycyclic Systems. Part III.*[1] *A Synthesis of 1 : 2 : 9-Trimethylpicene.*

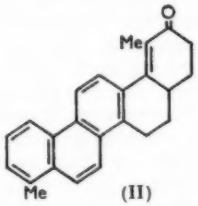
By D. NASIPURI.

SYNTHESIS of picene[1] by the Robinson ring-extension of 2-alkoxycarbonyl-1 : 2 : 3 : 4-tetrahydro-1-oxochrysene (*e.g.*, I; R = H) can be extended[2] to 1-substituted picenes by using β-chloro-ketones in place of the methiodide of Mannich bases. This method has now been used for the synthesis of 1 : 2 : 9-trimethylpicene (III), an expected dehydrogenation product of α-amyrin, on the basis of the structure proposed by Meisels, Jeger, and Ruzicka.[3]

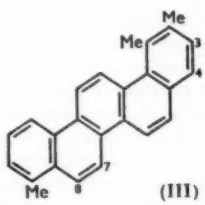
The sodio-derivative of the β-oxo-ester[2] (I; R = H) was condensed with 1-chloropentan-3-one;[4] the resultant dioxo-ester (I; R = CH_2·CH_2·COEt) on acidic hydrolysis afforded the unsaturated ketone (II) in good yield. Condensation with methylmagnesium iodide followed by dehydration and dehydrogenation with 30% palladium–charcoal then gave 1 : 2 : 9-trimethylpicene (III), characterised as 2 : 4 : 7-trinitrofluorenone complex and by its ultraviolet absorption.



(I)



(II)



(III)

This synthetic hydrocarbon, m. p. 266—268°, is found to be different from that, m. p. 306°, obtained in the dehydrogenation of α-amyrin,[5] the latter being apparently 2 : 9-dimethylpicene. Phillips and Tuites[6] also synthesised a trimethylpicene, m. p. 252—254°, which they represented by the same formulation (III), but their compound differs significantly from the present one particularly in the trinitrofluorenone complex. However, some of the steps in Phillips and Tuites's synthesis were not entirely free from ambiguity, the products of the last few steps not homogeneous, and the purity of the final compound was, therefore, questionable. The ultraviolet absorption spectra are very similar and it is probable that the trinitrofluorenone complex exists in polymorphs. We failed, however, to obtain a sample for comparison.

Experimental.—*1 : 2 : 3 : 4-Tetrahydro-2-methoxycarbonyl-7-methyl-1-oxo-2-3′-oxopentylchrysene* (I; R = CH_2·CH_2·COEt). To a cooled suspension of the sodio-derivative of the β-oxo-ester (I; R = H), prepared from methyl γ-(2-methoxycarbonyl-8-methyl-1-phenanthryl)-butyrate (4 g.), sodium methoxide (0·7 g.), and dry benzene (25 ml.), was added a solution of 1-chloropentan-3-one (4 g.) in benzene (15 ml.). The mixture was shaken for 1 hr., then left overnight, refluxed in the steam-bath for 30 min., and then decomposed with cold dilute sulphuric acid. The product, isolated in the usual way and crystallised from ethyl acetate (charcoal), gave the *ester* (I; R = CH_2·CH_2·COEt) (3 g.), m. p. 165—167° (Found: C, 77·2; H, 6·7. $C_{26}H_{26}O_4$ requires C, 77·6; H, 6·5%).

2 : 3 : 4 : 4a : 5 : 6-Hexahydro-1 : 9-dimethyl-2-oxopicene (II). The above dioxo-ester (2 g.), acetic acid (50 ml.), concentrated hydrochloric acid (25 ml.), and water (5 ml.) were refluxed under carbon dioxide for 20 hr., then cooled, and diluted with water. The *product* was filtered off, dried, passed in benzene through activated alumina, recovered, and crystallised from

[1] Parts I and II, *J.*, 1958, 2618, 2734.
[2] Roy and Nasipuri, *Science and Culture*, 1958, **24**, 34.
[3] Meisels, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 1075; 1950, **33**, 700.
[4] McMahon, Roper, Utermohlen, Hasek, Harris, and Brant, *J. Amer. Chem. Soc.*, 1948, **70**, 2971.
[5] Ruzicka and Morgeli, *Helv. Chim. Acta*, 1936, **19**, 377; Spring and Vickerstaff, *J.*, 1937, 249.
[6] Phillips and Tuites, *J. Amer. Chem. Soc.*, 1956, **78**, 5438.

benzene, forming plates (0·9 g.), m. p. 209—210° (Found: C, 88·1; H, 6·8. $C_{24}H_{22}O$ requires C, 88·3; H, 6·7%).

1 : 2 : 9-*Trimethylpicene* (III). The foregoing ketone (0·5 g.) in benzene was treated with excess of methylmagnesium iodide, and the crude product (0·55 g.) was heated with 30% palladium–charcoal [7] (100 mg.) at 340° for 1 hr. The melt was extracted with benzene, then filtered, and the solvent evaporated. The residue was passed in benzene–light petroleum through alumina and crystallised from ethanol–benzene, to give 1 : 2 : 9-trimethylpicene, plates, m. p. 266—268° (Found: C, 93·8; H, 6·3. Calc. for $C_{25}H_{20}$: C, 93·7; H, 6·3%), $\lambda_{max.}$ (in $CHCl_3$) 262, 281, 292, 326, 340, 365, 380, and 385 mμ (log ε 4·74, 4·83, 4·96, 4·36, 4·38, 3·70, 3·61, and 3·55 respectively). The 2 : 4 : 7-trinitrofluorenone complex crystallised from acetic acid as a red powder, m. p. 245—246° (Found: C, 71·9; H, 4·1; N, 6·85. Calc. for $C_{25}H_{20},C_{13}H_5O_7N_3$: C, 71·8; H, 3·9; N, 6·6%). Phillips and Tuites [6] give 252—254° and 203—205°.

The author is grateful to Mrs. Chhabi Dutta for microanalyses.

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[7] Linstead and Thomas, *J.*, 1940, 1127.

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846. *Chalcones and Related Compounds. Part VII.* Catalysed Exchange of Hydrogen Cyanide between Acetone Cyanohydrin and Chalcones.*

By B. E. BETTS and W. DAVEY.

NAZAROV and his co-workers [1] have described the addition of hydrogen cyanide to saturated and unsaturated carbonyl compounds by an exchange with acetone cyanohydrin. We have now used this reaction to add hydrogen cyanide to substituted chalcones (I) and other unsaturated ketones.

The optimum conditions for this exchange with chalcone itself were treatment of a solution in methanol with 3 mols. of acetone cyanohydrin and 0·1 mol. of 5—10% aqueous sodium carbonate. A 95% yield of the adduct (II; X = Y = H) was thus obtained. Use of triethylamine or saturated methanolic potassium hydroxide as catalyst resulted in lower yields. Reaction in dilute ethanolic solution with a tenfold excess of chalcone and saturated methanolic potassium hydroxide catalyst gave a 66% yield of 3-cyano-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-dione (III).[2]

$X{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}CO{\cdot}C_6H_4{\cdot}Y$ (I) $X{\cdot}C_6H_4{\cdot}CH(CN){\cdot}CH_2{\cdot}CO{\cdot}C_6H_4{\cdot}Y$ (II) $Ph{\cdot}CO{\cdot}CH_2{\cdot}CHPh{\cdot}CPh(CN){\cdot}CH_2{\cdot}CO{\cdot}Ph$ (III)

(IV) $Ph{\cdot}CH{:}CH{\cdot}CO{\cdot}Me$ $CO(CH{:}CH{\cdot}Ph)_2$ (VII)

(V) p-$(Ph{\cdot}CO{\cdot}CH{:}CH)_2C_6H_4$ m-$(Ph{\cdot}CO{\cdot}CH{:}CH)_2C_6H_4$ (VI)

By suitable modification of the optimum conditions a series of adducts (II) of alkyl-, alkoxy-, halogeno-, and dimethylamino-substituted chalcones (I) were prepared (see Table 1). Lower yields were again obtained when triethylamine was used as catalyst.

No crystalline products could be obtained from the exchange with 2′-, 3-, 3′-, 4-, and 4′-nitrochalcones, sodium carbonate catalyst being used. When triethylamine was used 3′-nitrochalcone gave a crystalline adduct, while the 2′-, 3-, 4-, and 4′-nitro-compounds were recovered unchanged.

The ketones (IV), (V), and (VI) gave good yields of the corresponding adducts. From

* Part VI, *J.*, 1958, 2606.

[1] Nazarov and Zavyalov, *J. Gen. Chem.* (*U.S.S.R.*), 1954, **24**, 475 (U.S. translation); Nazarov, Akhrem, and Kamernitsky, *ibid.*, 1955, **25**, 1291; see also Ames and Davey, *J.*, 1957, 3480; De Ruggieri, *Gazzetta*, 1957, **87**, 795; Spanish P. 229,413 (*Chem. Abs.*, 1957, **51**, 9723).

[2] Michael and Weiner, *J. Amer. Chem. Soc.*, 1937, **59**, 744.

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TABLE 1. *Hydrogen cyanide adducts.*

From substituted chalcones (I)

X	Y	Form *	Yield (%) †	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Found (%) Hal	Required (%) C	Required (%) H	Required (%) N	Required (%) Hal
H	H	Plates [a]	92	127° [1]	$C_{16}H_{13}ON$	—	—	—	—	—	—	—	—
p-Me	H	Plates [b]	99	137	$C_{17}H_{15}ON$	82·1	6·1	5·5	—	81·9	6·1	5·6	—
o-MeO	H	Prisms [b]	82	89	$C_{17}H_{15}O_2N$	76·7	5·6	5·3	—	77·0	5·7	5·3	—
m-MeO	H	Prisms [b]	83	112	$C_{17}H_{15}O_2N$	77·5	6·0	5·1	—	77·0	5·7	5·3	—
p-MeO	H	Plates [b]	81	119 [2]	$C_{17}H_{15}O_2N$	77·0	5·8	5·2	—	77·0	5·7	5·3	—
m-I	H	Needles	65	95	$C_{16}H_{12}ONI$	53·5	3·6	3·5	34·9	53·2	3·3	3·9	35·1
p-I	H	Needles	83	126	$C_{16}H_{12}ONI$	53·5	3·2	3·9	34·8	53·2	3·3	3·9	35·1
p-NMe_2	H	Yellow needles [c]	70	103	$C_{18}H_{18}ON_2$	77·5	6·3	9·7	—	77·7	6·5	10·1	—
H	*o*-Me	Needles [b]	94	95	$C_{17}H_{15}ON$	81·6	6·6	5·5	—	81·9	6·1	5·6	—
H	*p*-Cl	Needles	86	121 [3]	$C_{16}H_{12}ONCl$	71·0	4·8	5·4	12·9	71·2	4·5	5·2	13·1
H	*p*-Br	Prisms	89	125 [4]	$C_{16}H_{12}ONBr$	61·3	4·1	4·7	—	61·2	3·9	4·5	—
H	*p*-I	Needles	90	151	$C_{16}H_{12}ONI$	52·7	3·3	4·2	35·6	53·2	3·3	3·9	35·1
H	*m*-Cl	Needles	22	80	$C_{16}H_{12}ONCl$	70·5	4·5	5·3	13·1	71·2	4·5	5·2	13·1
H	*m*-Br	Needles	64	89	$C_{16}H_{12}ONBr$	60·9	3·9	4·4	25·8	61·2	3·9	4·5	25·4
H	*m*-I	Needles	87	104	$C_{16}H_{12}ONI$	53·2	3·8	3·9	34·5	53·2	3·3	3·9	35·1
H	*m*-NO_2	Needles [a]	62	128	$C_{16}H_{12}O_3N_2$	68·4	4·1	10·3	—	68·6	4·3	10·0	—
From other compounds													
(III)		Prisms [a]	66 [a]	237 [5]	$C_{31}H_{28}O_2N$	83·4	5·3	3·0	—	83·9	5·7	3·2	—
(IV)		Needles	54	46	$C_{11}H_{11}ON$	76·0	6·2	8·2	—	76·3	6·4	8·1	—
(V)		Prisms [a]	72	228	$C_{26}H_{20}O_2N_2,\frac{1}{2}H_2O$	78·2	5·1	7·1	—	77·8	5·3	7·0	—
(VI)		Prisms [a]	70	152	$C_{26}H_{20}O_2N_2,\frac{1}{2}H_2O$	78·3	5·2	7·1	—	77·8	5·3	7·0	—
(VII)	monoadduct	Plates	23 [d]	126	$C_{18}H_{15}ON$	82·3	5·7	5·7	—	82·7	5·8	5·4	—
(VII)	diadduct	Prisms	43	121	$C_{19}H_{16}ON_2$	78·9	5·1	9·9	—	79·1	5·6	9·7	—

* From light petroleum (b. p. 60—80°) unless otherwise stated: [a] From EtOH. [b] From MeOH. [c] From 2-ethoxyethanol.
† 10% Aqueous sodium carbonate was used as catalyst unless otherwise stated. [d] NEt_2. [e] Saturated KOH–MeOH.
[1] Mixed m. p. undepressed with authentic specimen. [2] Robertson and Stephen (*J.*, 1931, 863) give m. p. 118°. [3] Kohler and Shohan (*J. Amer. Chem. Soc.*, 1926, **48**, 2430) give m. p. 121°. [4] Allen and Frame (*Canad. J. Res.*, 1932, *6*, 605) give m. p. 124°. [5] Michael and Weiner (*J. Amer. Chem. Soc.*, 1937, **59**, 744) give m. p. 237°.

TABLE 2. *Ultraviolet absorption spectra (in ethanol) of hydrogen cyanide adducts (italic numerals denote an inflexion).*

Adducts from chalcones (I)

TABLE 2. *Ultraviolet absorption spectra (in ethanol) of hydrogen cyanide adducts (italic numerals denote an inflexion).*

Adducts from chalcones (I)

X	Y	$\lambda_{max.}$ (mμ)	ε	X	Y	$\lambda_{max.}$ (mμ)	ε	X	Y	$\lambda_{max.}$ (mμ)	ε	X	Y	$\lambda_{max.}$ (mμ)	ε
H	H	244	14,300	*m*-MeO	H	227	10,700	*p*-NMe_2	H	256	25,700	H	*m*-Cl	243	11,900
		268	1,300			244	14,200			*303*	3,000			290	1,900
		281	1,100			273	3,700			422	2,500	H	*m*-Br	245	11,700
p-Me	H	*221*	9,100			*281*	3,500	H	*o*-Me	255	16,200			290	1,700
		244·5	14,400	*p*-MeO	H	230	16,000	H	*p*-Cl	254	18,500	H	*m*-I	226	26,800
		273	1,700			244	14,700	H	*p*-Br	258	20,200			*250*	9,400
o-MeO	H	222	10,100			*248*	13,800			*263*	18,500			299	1,500
		244	14,400			275	2,900	H	*p*-I	*224*	8,600	H	*m*-NO_2	*208*	6,800
		273	4,200			282	2,700			269	18,100			229	9,900
		278	4,000	*m*-I	H	235·5	19,800			*276*	16,700			*260*	2,800
						244	17,000			307	1,300				
						279	2,000								
				p-I	H	237	25,800								
						244	17,000								
						278	1,400								

Adducts from other compounds

Compd.	$\lambda_{max.}$ (mμ)	ε	Compd.	$\lambda_{max.}$ (mμ)	ε	Compd.	$\lambda_{max.}$ (mμ)	ε	Compd.	$\lambda_{max.}$ (mμ)	ε
(III)	*218*	13,300	(IV)	*230*	30	(VII) monoadduct	222	10,600	(VII) diadduct	*242*	178
	244	14,200		*242*	77		*226*	10,200		*247*	236
	283	3,300		*247*	108		293	22,800		252	318
(V)	244	30,000		251·5	150					257·5	393
	273—82	3,400		257·5	186					264	313
(VI)	244	28,700		263·5	151					*267*	185
	274—82	2,400		*267*	86					*283*	57
				278	34						
				282	29						

TABLE 3. *Methyl esters derived from hydrogen cyanide adducts.*

Esters X·C_6H_4·CH(CO_2Me)·CH_2·CO·C_6H_4·Y

						Found (%)				Required (%)			
X	Y	Form [a]	Yield (%)	M. p.	Formula	C	H	N	Hal	C	H	N	Hal
p-Me	H	Plates	97	107°	$C_{18}H_{18}O_3$	76·1	6·6	—	—	76·6	6·4	—	—
m-MeO	H	Prisms	95	101	$C_{18}H_{18}O_4$	72·7	6·1	—	—	72·5	6·1	—	—
p-I	H	Plates	86	137	$C_{17}H_{15}O_3I$	51·6	3·9	—	31·6	51·8	3·8	—	32·2
p-NMe_2	H	Plates	81	105	$C_{19}H_{21}O_3N$	73·5	7·0	4·7	—	73·3	6·8	4·5	—
H	*o*-Me	Plates	98	88	$C_{18}H_{18}O_3$	76·9	6·6	—	—	76·6	6·4	—	—
H	*m*-I	Needles	70	73	$C_{17}H_{15}O_3I$	52·3	3·9	—	32·2	51·8	3·8	—	32·2
H	*p*-I	Needles	73	131	$C_{17}H_{15}O_3I$	51·8	3·6	—	32·7	51·8	3·8	—	32·2
H	*m*-NO_2	Needles	65	90	$C_{17}H_{15}O_5N$	64·9	4·9	4·5	—	65·2	4·8	4·5	—
Methyl esters from other adducts													
(VII) diadduct		Needles [c]	40	121	$C_{21}H_{22}O_5$	70·9	6·1	—	—	71·2	6·3	—	—
(V)		Prisms [b]	80	171	$C_{36}H_{36}O_6,\frac{1}{2}H_2O$	72·4	5·8	—	—	71·9	5·8	—	—
(VI)		Prisms [b]	82	155	$C_{36}H_{36}O_6$	72·8	5·7	—	—	73·3	5·7	—	—

[a] From methanol unless otherwise stated. [b] From light petroleum (b. p. 60—80°). [c] From 2-ethoxyethanol.

1 : 5-diphenylpenta-1 : 4-dien-3-one (VII), with aqueous sodium carbonate as catalyst there was obtained the diadduct, 1 : 5-dicyano-1 : 5-diphenylpentan-3-one, while the use of triethylamine gave the monoadduct, 1-cyano-1 : 5-diphenylpent-4-en-3-one. These structures were confirmed by the ultraviolet absorption spectra.

Starting material was recovered from attempted exchanges with 1-phenylhexa-1 : 3-dien-5-one and 1 : 9-diphenylnona-1 : 3 : 6 : 8-tetraen-5-one.

The ultraviolet absorption spectra are recorded in Table 2.

A number of the adducts were converted [3] into the corresponding methyl esters (Table 3).

Experimental.—Preparation of adducts. (i) To the compound (4 mol.) in acetone cyanohydrin (10 mol.) and methanol (sufficient to dissolve the compound) was added 10% aqueous sodium carbonate (1 mol.) or triethylamine (0·5 mol.); the mixture was refluxed for 1·5—4·0 hr. In most cases the product crystallised when the concentrated mixture cooled; otherwise the solution was poured into water, the product separating immediately.

(ii) Saturated methanolic potassium hydroxide (0·025 c.c. per g. of acetone cyanohydrin) was added to the compound dissolved in acetone cyanohydrin, and the mixture set aside overnight. The solution was then poured into water and the product collected.

THE POLYTECHNIC, 309 REGENT STREET, LONDON, W.1. [*Received, May 7th*, 1958.]

[3] Davey and Tivey, *J.*, 1958, 1230.

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847. *Some Properties of Solid Carbon Monosulphide.*

By M. A. P. HOGG and J. E. SPICE.

IT is well established that CS, obtained by the action of an electric discharge on carbon disulphide vapour, behaves as a normal, though unstable molecule in the gaseous state, rather than as a short-lived radical.[1] A brown substance described as polymeric CS condenses [2] when the gases from the discharge are cooled to liquid-nitrogen temperature. During investigations into the production of free radicals we repeated this experiment.

Experimental.—Carbon disulphide vapour, at a pressure of about 1 mm. flowing at about 0·5 mmole/min., was passed through a high-voltage A.C. glow discharge, and then through a trap cooled in liquid nitrogen. A narrow brown ring always formed about 1 cm. above the level of the liquid nitrogen, and in this region the temperature, as determined with a thermocouple, was about 135° K. Any unchanged carbon disulphide condensed above the brown ring. Below the ring was a whitish layer extending to about the level of the nitrogen, and lower still a colourless condensate.

Provided the layer of colourless condensate was sufficiently thin, it was quite stable at the temperature of liquid nitrogen, no change being observed (after the flow of gas had stopped) for up to 2 hr. With very thin layers, the colourless condensate gradually turned brown on warming, the rate of change depending on the rate of warming. With thicker layers, however, the change on warming was much more violent, being accompanied by a flash and a sharp report; a black deposit (presumably of carbon) was then observed as well as the brown substance. Whenever such an explosion occurred, the inside surface of the Pyrex trap became covered with numerous small cracks, sometimes extending right through the glass. The violence of the explosion was surprising: on one occasion when the total weight of product could not have exceeded 1 mg., and the total heat evolved could not therefore have exceeded a few calories, the thick trap was badly cracked. Presumably the layer of condensate was so thin, and the energy release so nearly adiabatic, that a very high temperature was attained instantaneously. Explosion normally occurred if the condensation was continued for more than a few minutes,

[1] For references, see Dyne and Ramsay, *J. Chem. Phys.*, 1952, **20**, 1055.
[2] *Idem, ibid.*; Dewar and Jones, *Proc. Roy. Soc.*, 1911, *A*, **85**, 574; Klemenc, *Z. Elektrochem.*, 1930, **36**, 722.

probably because the condensate was a poor conductor of heat, and its surface therefore became steadily warmer. If, however, the Dewar vessel was slowly raised, so as to spread the condensate over a larger area, it could be collected for as long as 20 min. before exploding. The amount of condensate probably never exceeded a few mmoles of CS. Attempts were made to collect the brown product directly, without explosion, by keeping the surface of the trap at 135° K. A heavy brown layer was formed, but explosion still occurred after about 12 min. The nature of the condensing surface was unimportant; normal condensation with explosion on warming occurred both in a trap packed with glass-wool, and on a nickel mirror. In the latter case there was no apparent reaction with the mirror.

We believe that the colourless deposit consisted of the compound CS, possibly as a glass, whereas the whitish layer was crystalline CS. By analogy with the b.p.s of CO, CO_2, and CS_2, molecular CS ought to condense at about 135° K. On warming a little above liquid-nitrogen temperature, it might polymerise to $(CS)_x$.

It was not possible to purify the polymeric deposit, but micro-analysis of the crude product gave C : S = 2·8 : 1, indicating that polymerisation was accompanied by considerable decomposition, with volatilisation of some sulphur.

Although gaseous CS is quite stable, for we have condensed it in a trap as far from the discharge as 1 m., or even in a trap attached to a side tube at some 30 cm. from the main gas stream, yet it completely decomposed on passage through 15 cm. of tubing packed with glass-wool at about 300° C. When boron trichloride vapour was introduced into the gas stream a brown film was condensed direct. CS condensed on solid ammonia without reaction, but when ethylene had been previously condensed in the collecting trap, the CS appeared to dissolve in the liquid ethylene, and no polymerisation occurred until all the liquid had evaporated.

In order to calculate the heat content changes of some processes involving CS, we use Cottrell's values [3] for bond-energy terms, corrected where necessary to the now generally-accepted value of 170 kcal./g.-atom for the heat of sublimation of carbon, and we ignore the difference between ΔH and ΔU. Thus, the heat of formation of gaseous CS from solid carbon and sulphur is: $\Delta H_f = -D(\mathrm{CS}) + 236$ kcal./mole. Gaydon [4] gives the heat of dissociation of CS as 166 ± 23 kcal./mole, so that ΔH_f for CS is $+70 \pm 23$ kcal./mole. The corresponding figure for CO is -27 kcal./mole. The heat of formation of solid CS would not, of course, differ from the above figure by more than a few kcal. A solid $(CS)_x$ polymer might consist of carbon chains cross-linked by sulphur atoms. On this basis, its heat of formation from gaseous CS would be $\Delta H_{\mathrm{polym.}} \sim -47 \pm 23$ kcal./mole of CS. Further, the heat of formation of the solid polymer from the elements would be $\Delta H_f \sim +20$ kcal./mole of CS, a value which may be compared with that of +13 kcal. derived by Dewar and Jones [2] from the heat of combustion of their brown product which, no doubt, had already partly decomposed into carbon and sulphur.

On the basis of these figures, there is no difficulty in accounting for the instability of CS or for its ease of polymerisation. The heat of polymerisation of CO to a solid with a structure analogous to that postulated for $(CS)_x$ would, on the other hand, be $\Delta H_{\mathrm{polym.}} = +7$ kcal./mole. This difference is due to the greater stability of multiple links between carbon and oxygen than of those between carbon and sulphur. The relative stability of gaseous CS is to be contrasted with its extreme reactivity as a solid, except at those very low temperatures at which it appears to be stabilised. The high reactivity of solid CS is probably due to the juxtaposition of the CS molecules in the condensate.

DEPARTMENT OF INORGANIC AND PHYSICAL CHEMISTRY,
UNIVERSITY OF LIVERPOOL. [*Received, May 28th*, 1958.]

[3] Cottrell, "The Strengths of Chemical Bonds," Butterworths, London, 1954.
[4] Gaydon "Dissociation Energies and Spectra of Diatomic Molecules," Chapman and Hall, London, 1953.

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848. *The Oxidation of Aromatic Amines. Part VII.* The Action of Persulphate on Some Aromatic Amines.*

By E. Boyland and Peter Sims.

The conversion, by alkaline persulphate, of a number of primary or tertiary aromatic amines into *o*-aminophenyl sulphates was described previously.[1] The oxidation has been extended to include the secondary amines, *N*-methylaniline and diphenylamine, and the heterocyclic amines 2- and 4-aminopyridine, all of which yield the corresponding *ortho*-substituted sulphuric esters. 4-Aminopyridine also yielded 4 : 4′-azoxypyridine.

4-Amino-2′ : 3-dimethyldiphenyl, which Walpole, Williams, and Roberts[2] showed to cause intestinal tumours in rats, yielded 4 : 4′-azo- and 4 : 4′-hydrazo-2′ : 3-dimethyldiphenyl as well as the expected sulphuric ester. 3 : 6 : 1- and 2 : 6 : 1-Xylidine also yielded sulphuric esters: with the latter amine, where both positions *ortho* to the amino-group are blocked by methyl groups, substitution by the entering sulphuric group in the *para*-position. All the above esters yielded the corresponding aminophenols on acid-hydrolysis.

Experimental.—The persulphate oxidations and the working up were carried out as previously described.[1]

Oxidation of N-*methylaniline.* This yielded *potassium* o-*methylaminophenyl sulphate* in plates (from methanol–ether) (1·2 g. from 5 g. of base) (Found: N, 5·7; S, 12·8. $C_7H_8O_4NSK$ requires N, 5·7; S, 13·3%). The ester with 2N-hydrochloric acid at 100°, in 15 min., yielded *o*-methylaminophenol, separating from light petroleum (b. p. 60—80°) in plates, m. p. 95—97° (lit.,[3] m. p. 96—97°) (Found: N, 11·4. Calc. for C_7H_9ON: N, 11·4%).

Oxidation of diphenylamine. The sulphuric ester from this oxidation formed a greenish gum, from which hydrolysis with 2N-hydrochloric acid yielded 2-hydroxydiphenylamine, prismatic needles (from water) (0·95 g. from 5 g. of base), m. p. 66—67° (lit.,[3] m. p. 69—70°) (Found: N, 7·7. Calc. for $C_{12}H_{11}ON$: N, 7·6%).

Oxidation of the aminopyridines. (*a*) Oxidation of 2-aminopyridine (5 g.) yielded a crude potassium salt, a strong aqueous solution of which was acidified with concentrated hydrochloric acid. The solid (1·2 g.) which separated was recrystallised four times from propan-1-ol–water, to yield 2-*amino*-3-*pyridyl hydrogen sulphate* in prisms, m. p. 222—224° (softening at 210°) (Found: C, 31·55; H, 3·2; N, 14·7; S, 17·15. $C_5H_6O_4N_2S$ requires C, 31·6; H, 3·2; N, 14·7; S, 16·85%). The ester (1 g.) in water (5 ml.) was heated to 100° for 15 min. with concentrated hydrochloric acid (1 ml.). A small excess of sodium hydrogen carbonate was added and the solution was extracted with ether for 4 hr. Removal of the ether afforded solid 2-amino-3-hydroxypyridine (0·48 g.), which crystallised from ethanol–light petroleum (b. p. 80—100°) in plates, m. p. 166—167° (lit.,[4] m. p. 163—167·5°) (Found: C, 54·2; H, 5·25; N, 25·4. Calc. for $C_5H_6ON_2$: C, 54·5; H, 5·5; N, 25·5%). The picrate separated from aqueous ethanol in yellow prisms, m. p. 256° (decomp.) (lit.,[4] m. p. 257°) (Found: N, 20·4. Calc. for $C_{11}H_9O_8N_5$: N, 20·65%). When 2-amino-3-hydroxypyridine in pyridine was treated with an excess of benzoyl chloride a *tribenzoyl derivative* was obtained; this separated from aqueous ethanol in needles, m. p. 169—170° (Found: C, 73·8; H, 4·4; N, 6·6. $C_{26}H_{18}O_4N_2$ requires C, 73·9; N, 6·6%).

(*b*) During oxidation of 4-aminopyridine (5 g.) orange plates (1·1 g.) separated: four recrystallisations from light petroleum (b. p. 80—100°) yielded 4 : 4′-azoxypyridine in yellow plates, m. p. 126—127° (lit.,[5] m. p. 125—126°) (Found: N, 27·9. Calc. for $C_{10}H_8ON_4$: N, 28·0%). When the product was heated with iron filings, 4 : 4′-azopyridine was formed, which separated from

* Part VI, Sims, *J.*, 1958, 44.

[1] Boyland, Manson, and Sims, *J.*, 1953, 3623; Boyland and Sims, *J.*, 1954, 980; Sims, *J.*, 1958, 44.

[2] Walpole, Williams, and Roberts, *Brit. J. Indust. Med.*, 1952, **9**, 255.

[3] Heilbron and Bunbury, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1943.

[4] Bojarka-Dahlig and Urbanski, *Prace Placowch Nank-Badawez Munsterstwa Przemyslu Chem.*, 1952, **1**, 1.

[5] Hertog, Henkens, and van Roon, *Rec. Trav. chim.*, 1952, **71**, 1145.

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water in red needles, m. p. 105° (lit.,[5] m. p. 107—108°) (Found: N, 30·3. Calc. for $C_{10}H_8N_4$: N, 30·4%).

The oxidation mixture was worked up in the usual manner, the sulphuric ester being obtained as in (*a*). *4-Amino-3-pyridyl hydrogen sulphate* (1·55 g.) crystallised from water in red-brown plates, m. p. 245—256° (decomp.) (Found: C, 31·9; H, 3·4; N, 14·6; S, 17·0%). The ester (500 mg.) in water (5 ml.) and concentrated hydrochloric acid (3 ml.) was heated to 100° for 15 min. and the solution was treated with a small excess of sodium hydrogen carbonate and extracted with butan-1-ol (3 × 50 ml.). The butanol extract was evaporated to dryness and the residue was extracted twice with hot ethanol–light petroleum (b. p. 80—100°) (1 : 10) (20 ml.). The combined extracts were evaporated almost to dryness; red crystals (95 mg.) of *4-amino-3-hydroxypyridine* separated; from ethanol–light petroleum (b. p. 80—100°) they formed pink crystals, m. p. 240—242° (Found: C, 54·6; H, 5·6; N, 25·35. $C_5H_6ON_2$ requires C, 54·5; H, 5·5; N, 25·4%). Benzoylation with an excess of benzoyl chloride in pyridine yielded a *tribenzoyl derivative*, which formed needles (from aqueous ethanol), m. p. 144—145° (Found: C, 73·7; H, 4·54; N, 6·7).

Oxidation of 4-amino-2′ : 3-dimethyldiphenyl. The amine (2·26 g.) was oxidised with persulphate as before. The reddish-brown solid (1·85 g.) which separated overnight was collected and dissolved in a minimum of boiling ethanol. The plates which separated on cooling were recrystallised from ethanol, to yield *4 : 4′-azo-2′ : 3-dimethyldiphenyl* (590 mg.) in red plates with a golden lustre, m. p. 164° (Found: C, 86·6; H, 7·05; N, 7·1. $C_{28}H_{26}N_2$ requires C, 86·1; H, 6·7; N, 7·2%). The crystallisation mother-liquors were evaporated to small volume and allowed to crystallise. The product was recrystallised from ethanol to yield *4 : 4′-hydrazo-2′ : 3-dimethyldiphenyl* (140 mg.) in plates, m. p. 211° (Found: C, 85·7, 85·4; H, 7·6, 7·1; N, 7·1. $C_{28}H_{28}N_2$ requires C, 85·7; H, 7·2; N, 7·1%). Evaporation of the mother-liquors afforded a brown amorphous solid which was not further investigated.

The mother-liquors from the oxidation were evaporated to about 150 ml. under reduced pressure and washed with ether. The evaporation was continued until crystals separated. These were collected and recrystallised from aqueous ethanol to yield *potassium 4-amino-2′ : 3-dimethyl-5-diphenylyl sulphate* (850 mg.) in plates (Found: C, 50·3; H, 4·6; N, 4·2; S, 9·6; K, 11·9. $C_{14}H_{14}O_4NSK$ requires C, 50·7; H, 4·3; N, 4·2; S, 9·7; K, 11·8%). The ester, hydrolysed with hydrochloric acid, yielded *4-amino-5-hydroxy-2′ : 3-dimethyldiphenyl*, needles [from light petroleum (b. p. 80—100°)], m. p. 184—185° (Found: C, 78·8; 4, 7·1; N, 6·55. $C_{14}H_{15}ON$ requires C, 78·8; H, 7·1; N, 6·6%).

Oxidation of the xylidines. (*a*) *3 : 6 : 1-Xylidine* (5 g.) yielded *potassium 2-amino-3 : 6-dimethylphenyl sulphate* (2·2 g.), separating from 90% aqueous ethanol in plates (Found: C, 37·5; H, 3·9; N, 5·3. $C_8H_{10}O_4NSK$ requires C, 37·6; H, 3·95; N, 5·5%). Acid-hydrolysis yielded 2-amino-3 : 6-dimethylphenol, separating from benzene in pinkish plates, m. p. 147—149° (lit.,[3] m. p. 149—150°) (Found: N, 10·2. Calc. for $C_8H_{11}ON$: N, 10·2%), which formed a dibenzoyl derivative as needles (from aqueous ethanol), m. p. 177—178° (lit.,[3] m. p. 178—179°) (Found: N, 4·3. Calc. for $C_{22}H_{19}O_3N$: N, 4·1%).

(*b*) *2 : 6 : 1-Xylidine* (5 g.) yielded *potassium 4-amino-3 : 5-dimethylphenyl sulphate* (1·9 g.), separating from aqueous ethanol in flat needles (Found: C, 37·8; H, 4·1; N, 5·45; S, 12·3%). When a strong aqueous solution of the potassium salt (prepared either as above or from the free acid) was acidified with concentrated hydrochloric acid, feathery needles separated, which rapidly changed to short rods. *4-Amino-3 : 5-dimethylphenyl hydrogen sulphate* recrystallised from aqueous ethanol in rods, m. p. 258—259° (decomp.) (darkening at 246°) (Found: N, 6·2; S, 14·4. $C_8H_{11}O_4NS$ requires N, 6·45; S, 14·8%).

Acid-hydrolysis of the ester yielded 4-amino-3 : 5-dimethylphenol, plates (from chloroform), m. p. 180—181° (lit.,[3] m. p. 181°) (Found: N, 10·35%).

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849. *Acid-stable Organic Azides, and the Schmidt Reaction with Heterocyclic Ketones.*

By M. M. Coombs.

The behaviour [1] of 9-azido-9-methylfluorene indicates that in sulphuric acid an equilibrium exists between the proton-adduct of the azide, the 9-methylfluorenyl cation, and hydrazoic acid. An azide which gives rise to a stable carbonium ion should tend to be stable to acids, since the $>C\overset{\curvearrowright}{-}N_3H^+$ bond will break rather than the $-N\overset{\curvearrowright}{-}N^+\equiv N$ bond. The inertness of triphenylmethyl azide [2] and the stability of the triphenylmethyl cation support this conclusion. Delocalisation of the positive charge over the heterocyclic ring gives a high degree of stability to the 9-phenyl-xanthenyl and -thiaxanthenyl cations [3] and it was of interest to study the azides derived from these. When this work was nearing completion Loudon *et al.*[4] described the preparation and thermal decomposition of these azides. Our results are essentially similar, and are summarised in the Experimental section; various other observations concerning the stability of these azides are now reported.

9-Azido-9-phenylxanthen dissolved in sulphuric acid with the yellow colour and green fluorescence characteristic of the 9-phenylxanthenyl cation. The presence of freely available hydrazoic acid was demonstrated by the formation of phenanthridone when fluorenone was added to the solution, and on dilution of this mixture with water 9-hydroxy-phenylxanthen was isolated in good yield. The azide was largely recovered when its solution in sulphuric acid was poured into water, and, even after 24 hours' treatment, no rearrangement products were detected. The deep red colour of the 9-phenylthiaxanthenyl cation was shown by a solution of 9-azido-9-phenylxanthen in sulphuric acid and, similarly, the azide was recovered almost quantitatively. Inhibition of delocalisation of the positive charge on $C_{(9)}$ was expected to decrease this stability and, indeed, this was found with 9-hydroxy-9-phenylthiaxanthen dioxide which reacted readily with hydrazoic and sulphuric acid with evolution of nitrogen and formation of thiaxanthone dioxide anil in high yield. The same product was formed when the sulphone was added to a sulphuric acid solution of 9-azido-9-phenylthiaxanthen, thus proving the availability of hydrazoic acid in this solution. The anil, rather than the isomeric ring-enlarged thiazepine dioxide, is to be expected [5] since the electron-density is greater in the $C_{(9)}$–Ph bond than in the bonds joining the condensed benzene rings to $C_{(9)}$, owing to the strong electron-withdrawal by the *ortho*-substituent in these rings.

Jones and Mann [6] have pointed out that charge separation in heterocyclic ketones lowers the frequency of the infrared carbonyl band. Xanthone and thiaxanthone absorb at 1660 and 1645 cm.$^{-1}$ respectively, and therefore considerable delocalisation of the positive charge from the carbonyl group is to be expected in sulphuric acid solution. The failure of these ketones to undergo the Schmidt reaction while thiaxanthone dioxide, which shows a normal carbonyl adsorption at 1684 cm.$^{-1}$, reacts quantitatively to give the lactam of 2-amino-2′-carboxydiphenyl sulphone, confirms this expectation. Also Caronna and Palazzo's observation [7] that anthrone (1656 cm.$^{-1}$) does not react with hydrazoic and sulphuric acid whereas anthraquinone (1684 cm.$^{-1}$) gives the lactam of 2-aminobenzophenone-2′-carboxylic acid has been confirmed. Thus an abnormally low carbonyl frequency indicates that a ketone will not undergo the Schmidt reaction. However, the opposite is not true. Thus fluorenone (1715 cm.$^{-1}$) reacts readily to give phenanthridone, but the

[1] Coombs, *J.*, 1958, **3454**.
[2] Senior, *J. Amer. Chem. Soc.*, 1916, **38**, 2718.
[3] Elderfield, "Heterocyclic Compounds," John Wiley and Sons, Inc., New York, 1951, Vol. II, pp. 469, 477, 546—547.
[4] Galt, Loudon, and Sloan, *J.*, 1958, 1588.
[5] Arcus and Coombs, *J.*, 1954, 4319.
[6] Jones and Mann, *J.*, 1958, 294.
[7] Caronna and Palazzo, *Gazzetta*, 1953, **83**, 533.

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reaction fails with 4 : 5-diazafluorenone which has almost the same carbonyl frequency (1718 cm.$^{-1}$). Presumably with this compound protonation occurs at one of the ring-nitrogen atoms rather than at the carbonyl group. Similar behaviour is exhibited by the pyridinecarboxylic acids, anthranilic acid, and the aliphatic amino-acids, with which the reaction fails.[8]

Experimental.—98% Sulphuric acid was used thoughout.

9-Azido-9-phenylxanthen. This compound was obtained quantitatively when 9-hydroxy-9-phenylxanthen (5 g.) was stirred with sodium azide (5 g.), trichloroacetic acid (50 g.), and chloroform (50 ml.). It formed needles (from light petroleum), m. p. 114—115° (Found: C, 76·3; H, 4·1; N, 14·3. Calc. for $C_{19}H_{13}ON_3$: C, 76·25; H, 4·4; N, 14·05%). Loudon [4] reports m. p. 110°.

The bright yellow solution of this azide (2·00 g.) in sulphuric acid (3 ml.) and chloroform (15 ml.) was stirred for 8 hr. at room temperature and left for a further 16 hr. The mixture was poured into water and shaken, and the chloroform layer was washed with sodium hydrogen carbonate solution and dried (Na_2SO_4). Evaporation left a crystalline solid (1·94 g.) which on fractional crystallisation from light petroleum gave the azide (1·32 g.), m. p. 102—107° and mixed m. p. 102—108°, and 9-hydroxy-9-phenylxanthen (0·11 g.), m. p. and mixed m. p. 158°. When this experiment was repeated, but with stirring for 2½ hr., the azide (1·46 g.), m. p. 105—111° and mixed m. p. 106—112°, was recovered.

The azide (300 mg.) in sulphuric acid (3 ml.) was stirred at 25° while fluorenone (170 mg.) was added during ½ hr., and stirring was continued for a further 2½ hr. The dark mixture was then diluted with ice (10 g.), and the cream solid was collected and crystallised from ethanol, yielding phenanthridone (110 mg.), m. p. and mixed m. p. 294—295°. The yellow filtrate was further diluted with water (100 ml.) and the white precipitate of 9-hydroxy-9-phenylxanthen was collected and dried; it amounted to 180 mg. and had m. p. and mixed m. p. 156—157°.

9-Azido-9-phenylthiaxanthen.—9-Hydroxy-phenylthiaxanthen, stirred with sodium azide, trichloroacetic acid, and chloroform, yielded *9-azido-9-phenylthiaxanthen*, tablets (from light petroleum), m. p. 57° (Found: C, 72·55; H, 4·5; N, 13·1. $C_{19}H_{13}N_3S$ requires C, 72·35; H, 4·15; N, 13·3%). This azide (2·00 g.) was stirred with sulphuric acid and chloroform as described above, and the red solution was diluted with water after 24 hr. The chloroform solution, on evaporation, gave a crystalline mass (1·93 g.), m. p. 49—52°, and 51—55° when mixed with the pure azide.

Reactions with 9-hydroxy-9-phenylthiaxanthen dioxide. This sulphone (2·00 g.; m. p. 214—216° [9]) was added portionwise to a vigorously stirred mixture of sodium azide (1 g.), sulphuric acid (3 ml.), and chloroform (20 ml.) at 25° during 1 hr. Nitrogen was evolved and the sulphuric acid became deep yellow. After a further 2 hr. the mixture was diluted with ice and water, and the chloroform layer was washed with water and dried ($MgSO_4$). Removal of the solvent gave a solid (1·85 g.) which was recrystallised from ethanol. *Thiaxanthone dioxide anil* formed yellow prisms (1·65 g.), m. p. 236—237° (Found: C, 71·4; H, 4·3; N, 4·5. $C_{19}H_{13}O_2NS$ requires C, 71·45; H, 4·1; N, 4·4%).

The anil (0·5 g.) was heated on the steam-bath with 5N-hydrochloric acid (30 ml.) until all the colour was discharged, and the solid was collected and dried. It (0·32 g.) had m. p. 188° alone and when mixed with thiaxanthone dioxide.

9-Hydroxy-9-phenylthiaxanthen dioxide (0·5 g.) was added to the red solution of 9-azido-9-phenylthiaxanthen (0·5 g.) in sulphuric acid (5 ml.) at 25° with stirring during ½ hr.: nitrogen was evolved after each addition. After an additional 2 hr. the mixture was added to an excess of ice-cold 2N-sodium carbonate, and the suspension was extracted with chloroform. Evaporation of the dried ($MgSO_4$) extract gave a resinous yellow solid from which thiaxanthone dioxide anil (0·33 g.), m. p. 133° alone and 136—137° when mixed with the pure specimen, was obtained by recrystallisation from ethanol.

Thermal decomposition. 9-Azido-9-phenylxanthen (1·00 g.) was heated at 170° for 2 hr. in decalin (10 ml.). Evaporation of the orange solution and fractional crystallisation of the residue gave 11-phenyldibenz[*b*,*f*]-1 : 4-oxazepine (0·56 g.), m. p. 109—110° after recrystallisation from methanol (Found: C, 84·4; H, 5·1; N, 5·15. Calc. for $C_{19}H_{13}ON$: C, 84·1; H, 4·85;

[8] Smith, "Organic Reactions," John Wiley and Sons, Inc., New York, 1946, Vol. III, p. 312.
[9] Gomberg and Britton, *J. Amer. Chem. Soc.*, 1921, **43**, 1946.

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N, 5·15%), and xanthone anil (0·22 g.), m. p. 136—138°. Loudon [4] reports m. p.s 108° and 135° for these two compounds. The anil (100 mg.), on hydrolysis with 5N-hydrochloric acid, gave xanthone (60 mg.), m. p. 174—176° and mixed m. p. 176—178°.

Similarly 9-azido-9-phenylthiaxanthen (3·6 g.) gave thiaxanthone anil (2·1 g.), m. p. 150°, which on hydrolysis yielded thiaxanthone, m. p. and mixed m. p. 212° (210 mg. from 300 of anil). The dark mother-liquors were concentrated and chromatographed on alumina with light petroleum (b. p. 40—60°), from which was isolated pale yellow needles of 11-phenyldibenzo[*b*,*f*]-1 : 4-thiazepine (0·3 g.), m. p. 116—117°. Loudon [4] reports m. p. 117° for this compound, and 153° for the anil.

Schmidt reactions with the ketones. The ketone (1·00 g.) in sulphuric acid (10 ml.) was stirred at 30° while sodium azide (1 g.) was added during 2 hr. Next day, the mixture was poured into water, and the product was collected and dried.

Anthraquinone gave the lactam of 2-aminobenzophenone-2′-carboxylic acid (1·00 g.), m. p. 243—245°. Recrystallisation from acetic acid yielded needles, m. p. 250—251° (Found: N, 6·35. Calc. for $C_{14}H_9O_2N$: N, 6·25%). Caronna *et al.*[7] report m. p. 245°.

Thiaxanthone dioxide gave 2-amino-2′-carboxydiphenyl sulphone lactam (1·05 g.), m. p. 290—292° (Found: N, 5·25. Calc. for $C_{13}H_9O_3NS$: N, 5·4%). McClelland and Peters [10] record m. p. 290° for this compound prepared by the cyclisation of the amino-acid.

The following ketones were recovered (weight, m. p. of the recovered material, and mixed m. p.): Anthrone (0·95 g., 155°, 155—157°); xanthrone (0·95 g., 177—179°, 176—178°); thiaxanthone (0·95 g.; 214—216°, 215—216°); 4 : 5-diazafluorenone (m. p. 211° [11]) (0·81 g., 205—207°; 207—209°).

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South Kensington, London, S.W.7. [*Received, June 6th*, 1958.]

[10] McClelland and Peters, *J.*, 1947, 1229.
[11] Smith, *J. Amer. Chem. Soc.*, 1950, **72**, 842.

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850. *Thiophen Derivatives. Part XIII.* Some Reactions of 3-Methylthiophen.*

By J. Lamy, Denise Lavit, and Ng. Ph. Buu-Hoï.

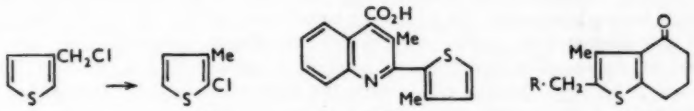
3-Methylthiophen, now available commercially, has become the most accessible source for many 3-substituted thiophens, 3-bromomethylthiophen, for instance, the product of its side-chain bromination with *N*-bromosuccinimide,[1] being an important intermediate. It has now been found that chlorination with *N*-chlorosuccinimide, even in the presence of benzoyl peroxide, gives mainly 2-chloro-3-methylthiophen (II), along with negligible amounts of the expected 3-chloromethylthiophen (I), probably because of allylic rearrangement of the latter under the influence of the succinimide formed in the reaction. This is in line with an earlier record of the rearrangement of 2-bromomethyl-5-methylthiophen to 3-bromo-2 : 5-dimethylthiophen catalysed by another weak alkali, cuprous cyanide.[2]

It is known that 3-methylthiophen undergoes acetylation with acetic anhydride in the presence of phosphoric acid, to give a mixture of mainly 2-acetyl-3-methylthiophen and some of the 4-methyl isomer;[3] however, its formylation with dimethylformamide in

* Part XII, Buu-Hoï, *J.*, 1958, 2418.

[1] Cf. Buu-Hoï, *Annalen*, 1944, **556**, 1; Buu-Hoï and Lecocq, *Compt. rend.*, 1946, **222**, 1441; Campaigne and Le Suer, *J. Amer. Chem. Soc.*, 1948, **70**, 1556; Dittmer, Martin, Hertz, and Cristol, *ibid.*, 1949, **71**, 1201.
[2] Lecocq and Buu-Hoï, *Compt. rend.*, 1947, **224**, 658.
[3] Hartough and Kosak, *J. Amer. Chem. Soc.*, 1947, **69**, 3093; Hartough and Conley, *ibid.*, p. 3096.

the presence of phosphorus oxychloride now yielded only 3-methyl-2-thenaldehyde. This aldehyde failed to react with thiosemicarbazide, although 5-ethyl-4-methyl-2-thenaldehyde readily gave a thiosemicarbazone; this abnormality recalls the inability, ascribed to steric hindrance, of 2-acetyl-3-ethylthionaphthen to give a semicarbazone or to undergo



(I) (II) (III) (IV)

Pfitzinger reactions.[4] It is to be noted, however, that 2-acyl-3-methylthiophens gave normal Pfitzinger reactions, 3-methyl-2-propionylthiophen, for instance, affording 3-methyl-2-(3-methyl-2-thienyl)cinchoninic acid (III) which, on thermal decarboxylation, yielded the corresponding quinoline; similar cinchoninic acids and quinolines were obtained from 2-acetyl-4-methylthiophen.

2 : 3-Dimethyl-, 2-ethyl-3-methyl-, 2-ethyl-4-methyl-, and 2-ethyl-4 : 5-dimethylthiophen (the two last-named being new) were readily prepared by Wolff–Kishner reduction of the corresponding oxo-compounds. Succinoylation of 2 : 3-dimethylthiophen and 2-ethyl-3-methylthiophen, and reduction of the resulting keto-acids, yielded the substituted butyric acids, whose cyclisation afforded 4 : 5 : 6 : 7-tetrahydro-2 : 3-dimethyl-4-oxo- (IV; R = H) and 2-ethyl-4 : 5 : 6 : 7-tetrahydro-3-methyl-4-oxo-thianaphthen (IV; R = Me).

Experimental.—Acetylation and formylation of 3-methylthiophen. (*a*) Reaction of 3-methylthiophen (98 g.) with acetic anhydride (122 g.) in the presence of phosphoric acid (5 g.), performed according to Hartough *et al.*,[5] afforded a 90% total yield of 2-acetyl-3-methylthiophen (93·5 g.), b. p. 98—99°/14 mm., and the 4-methyl isomer (33 g.), b. p. 108—109°/14 mm.

(*b*) Reaction of 3-methylthiophen (98 g.) with dimethylformamide (84 g.) in the presence of phosphoric oxychloride (200 g.), performed in the usual way,[6] gave as sole product 3-methyl-2-thenaldehyde (88·5 g.), b. p. 112—113°/24 mm., $n_D^{20\cdot5}$ 1·6013; no thiosemicarbazone was obtained, even on prolonged heating in ethanol.

Preparation of 2-ethyl-3- and -4-methylthiophen. The appropriate ketone (10 g.) and 98% hydrazine hydrate (10 g.) in diethylene glycol (30 c.c.) were heated for a few minutes at 80° to allow the hydrazone to be formed, potassium hydroxide (10 g.) was then added, and the mixture was boiled until the product had ceased to distil off (3 hr.). The distillate was extracted in ether, washed with dilute hydrochloric acid, then with water, dried ($CaCl_2$), recovered, and fractionated. An 83% yield was obtained of 2-ethyl-3-methylthiophen, b. p. 158—161°, $n_D^{22\cdot5}$ 1·5225, and of *2-ethyl-4-methylthiophen*, b. p. 160—161°, $n_D^{22\cdot5}$ 1·5218 (Found: C, 66·7; H, 8·0. $C_7H_{10}S$ requires C, 66·7; H, 8·0%). 2 : 3-Dimethylthiophen, b. p. 142—143°, $n_D^{22\cdot5}$ 1·5250, was prepared in the same way, in 66% yield, from 3-methyl-2-thenaldehyde.

5-Ethyl-4-methyl-2-thenaldehyde. To an ice-cooled mixture of 2-ethyl-3-methylthiophen (25 g.) and dimethylformamide (15 g.), phosphorus oxychloride (50 g.) was added dropwise with stirring; after the reaction had subsided, the mixture was refluxed on a water-bath for 1 hr. and, after cooling, was shaken with 25% aqueous sodium acetate (200 c.c.). The product was taken up in chloroform, washed successively with dilute hydrochloric acid, 5% aqueous sodium carbonate, and water, dried (Na_2SO_4), recovered, and fractionated *in vacuo*. The *aldehyde* (18 g.) had b. p. 126—127°/14 mm., n_D^{22} 1·5809 (Found: C, 62·3; H, 6·5. $C_8H_{10}OS$ requires C, 62·3; H, 6·5%). The *thiosemicarbazone*, prepared by briefly heating an ethanolic solution of the aldehyde with thiosemicarbazide, formed pale yellow prisms, m. p. 203°, from ethanol (Found: N, 18·4. $C_9H_{13}N_3S_2$ requires N, 18·5%).

[4] Buu-Hoï and Cagniant, *Ber.*, 1943, **76**, 1269; for similar observations in the benzofuran group, see Bisagni, Buu-Hoï, and Royer, *J.*, 1955, 3688.

[5] Cf. Steinkopf, "Die Chemie des Thiophens," Steinkopff, Dresden and Leipzig, 1941, p. 53.

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2-Ethyl-3 : 5-dimethylthiophen. This *compound* (8 g.), prepared by reduction of the foregoing aldehyde (15 g.) with hydrazine hydrate (15 g.) and potassium hydroxide (10 g.) in diethylene glycol (50 c.c.), had b. p. 179—180°, $n_D^{22\cdot5}$ 1·5158 (Found: C, 68·4; H, 8·6. $C_8H_{12}S$ requires C, 68·5; H, 8·6%).

Chlorination of 3-methylthiophen with N-chlorosuccinimide. A stirred mixture of 3-methylthiophen (55 g.), *N*-chlorosuccinimide (67 g.), and dry carbon tetrachloride (160 c.c.) was refluxed with benzoyl peroxide (0·5 g.) for 12 hr.; after cooling, the succinimide formed was filtered off and washed with carbon tetrachloride, the filtrate evaporated off, and the residue fractionated *in vacuo*. The lower-boiling portion consisted of 2-chloro-3-methylthiophen [5] (II) (20 g.), b. p. 53—54°/15 mm., $n_D^{24\cdot5}$ 1·5529; the higher-boiling portion consisted of *3-chloromethylthiophen* (I), a lachrymatory oil with a pungent odour (1·5 g.), b. p. 74—75°/14 mm. (Found: C, 45·0; H, 3·5. C_5H_5SCl requires C, 45·3; H, 3·8%).

3-Methyl-2-(3-methyl-2-thienyl)cinchoninic acid (III). A solution of 3-methyl-2-propionylthiophen [6] (3 g.), isatin (3 g.), and potassium hydroxide (3·3 g.) in ethanol (25 c.c.) was gently refluxed for 24 hr.; the solvent was then distilled off, the residue taken up in water, the neutral impurities were extracted in ether, and the aqueous layer was acidified with acetic acid. The *acid* formed yellowish prisms, m. p. 241—242°, from ethanol (Found: C, 67·5; H, 4·5. $C_{16}H_{13}O_2NS$ requires C, 67·8; H, 4·6%). *3-Methyl-2-(3-methyl-2-thienyl)quinoline*, obtained by heating this acid above its m. p. and distilling the residue *in vacuo*, formed yellowish prisms, m. p. 67—68°, from ethanol (Found: N, 6·1. $C_{15}H_{13}NS$ requires N, 5·9%).

2-(4-Methyl-2-thienyl)cinchoninic acid. Prepared from 2-acetyl-4-methylthiophen (4·6 g.), isatin (5·5 g.), and potassium hydroxide (5·6 g.) in ethanol (60 c.c.; 4 hours' refluxing), this *acid* (5·2 g.) formed yellow prisms, m. p. 233° (Found: C, 66·9; H, 4·0. $C_{15}H_{11}O_2NS$ requires C, 66·9; H, 4·1%). *2-(4-Methyl-2-thienyl)quinoline* crystallised as colourless prisms, m. p. 159° (Found: N, 6·4. $C_{14}H_{11}NS$ requires N, 6·2%), giving a picrate, yellow leaflets, m. p. 224—225°, from ethanol.

6-Methyl-2-(4-methyl-2-thienyl)cinchoninic acid. Prepared from 2-acetyl-4-methylthiophen (1·5 g.), 5-methylisatin (2 g.), and potassium hydroxide (2 g.), this *acid* (2 g.) formed yellowish needles, m. p. 220°, from ethanol (Found: C, 67·5; H, 4·6. $C_{16}H_{13}O_2NS$ requires C, 67·8; H, 4·6%). *6-Methyl-2-(4-methyl-2-thienyl)quinoline* formed colourless needles, m. p. 115°, from ethanol (Found: N, 5·7. $C_{15}H_{13}NS$ requires N, 5·9%), giving a *picrate*, yellow leaflets, m. p. 198—199°, from ethanol (Found: N, 11·8. $C_{21}H_{16}O_7N_4S$ requires N, 12·0%).

β-(4 : 5-Dimethyl-2-thenoyl)propionic acid. To an ice-cooled solution of 2 : 3-dimethylthiophen (48 g.) and succinic anhydride (48 g.) in nitrobenzene (350 c.c.), aluminium chloride (150 g.) was added in small portions with stirring, and the brown-red mixture left for 16 hr. at room temperature; after decomposition with ice and steam-distillation the solid product was purified by dissolution in aqueous sodium carbonate and reprecipitation with hydrochloric acid. The *keto-acid* (69 g.) formed colourless prisms, m. p. 161°, from *cyclo*hexane–benzene (Found: C, 56·7; H, 5·6. $C_{10}H_{12}O_3S$ requires C, 56·6; H, 5·7%).

γ-(4 : 5-Dimethyl-2-thienyl)butyric acid. The foregoing acid (70 g.), potassium hydroxide (60 g.), and hydrazine hydrate (70 g.) in warm diethylene glycol (300 c.c.) were refluxed for 6 hr. with removal of water. After cooling and dilution with water, acidification with hydrochloric acid furnished a product which was taken up in chloroform and purified by distillation *in vacuo*. The *acid* (32 g.) formed colourless prisms, b. p. 213—214°/40 mm., m. p. 44° (from *cyclo*hexane) (Found: C, 60·5; H, 7·1. $C_{10}H_{14}O_2S$ requires C, 60·6; H, 7·1%).

4 : 5 : 6 : 7-Tetrahydro-2 : 3-dimethyl-4-oxothionaphthen (IV; R = H). γ-(4 : 5-Dimethyl-2-thienyl)butyryl chloride, prepared from the above acid (30 g.), thionyl chloride (13 c.c.), and pyridine (6 drops) in dry ether (100 c.c.), formed a pale yellow oil (15 g.), b. p. 150—151°/18 mm. To a solution of this acid chloride (15 g.) in dry carbon disulphide (150 c.c.), stannic chloride (11 c.c.) was added in small portions with stirring, and the mixture refluxed for 3 hr. After cooling and decomposition with ice and hydrochloric acid, the product was taken up in chloroform, the organic layer washed with aqueous sodium carbonate, then with water, dried (Na_2SO_4), and evaporated, and the residue fractionated *in vacuo*. The *ketone* (6·5 g.) formed colourless prisms, b. p. 153—154°, m. p. 48—49°, from *cyclo*hexane (Found: C, 61·2; H, 6·2. $C_{10}H_{12}OS$ requires C, 61·2; H, 6·2%). The *semicarbazone* crystallised as needles, m. p. 199°, from ethanol (Found: N, 17·5. $C_{11}H_{15}ON_3S$ requires N, 17·7%).

[6] Cf. Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1949, **68**, 5.

β-(*5-Ethyl-4-methyl-2-thenoyl*)*propionic acid.* Prepared as for the lower homologue, from 2-ethyl-3-methylthiophen (23 g.), succinic anhydride (25 g.), and aluminium chloride (70 g.) in nitrobenzene (120 c.c.), this *acid* crystallised as colourless prisms (23 g.), m. p. 128°, from toluene (Found: C, 58·7; H, 6·1. $C_{11}H_{14}O_3S$ requires C, 58·4; H, 6·2%).

γ-(*5-Ethyl-4-methyl-2-thienyl*)*butyric acid.* Prepared from the foregoing acid (22 g.) with hydrazine hydrate (22 g.) and potassium hydroxide (22 g.) in diethylene glycol (120 c.c.), this *acid* (13 g.) formed a pale yellow oil, b. p. 193—195°/14 mm. (Found: C, 62·2; H, 7·6. $C_{11}H_{16}O_2S$ requires C, 62·3; H, 7·6%). The corresponding chloride (8·5 g.), prepared from the acid (13 g.) with thionyl chloride (6 c.c.) and pyridine (3 drops) in ether (50 c.c.), had b. p. 159—161°/12 mm. Cyclisation of this chloride (8 g.) with stannic chloride (6 c.c.) in carbon disulphide furnished 2-*ethyl*-4 : 5 : 6 : 7-*tetrahydro*-3-*methyl*-4-*oxothionaphthen* (IV; R = Me) (5 g.), b. p. 164—165°/16 mm. (Found: C, 67·9; H, 7·3. $C_{11}H_{14}OS$ requires C, 68·0; H, 7·3%).

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851. *Kinetics of the Reaction of Methyl Radicals with Toluene.*

By S. J. W. PRICE and A. F. TROTMAN-DICKENSON.

WHEN a metal alkyl is pyrolysed in the presence of a large excess of toluene, methane is formed by reaction (1) and ethane by reaction (2):

$$CH_3\cdot + C_6H_5\cdot CH_3 = CH_4 + C_6H_5\cdot CH_2\cdot \quad \ldots\ldots\ldots\ldots (1)$$

$$2CH_3\cdot = C_2H_6 \quad \ldots\ldots\ldots\ldots\ldots\ldots (2)$$

The decompositions of dimethyl-mercury, -cadmium,[1a] and -zinc,[1b] trimethyl-bismuth and -antimony, and dimethyltin dichloride,[1c] all of which yield methyl radicals, have recently been studied. From the complete analytical results [2] we have calculated the rate constant of reaction (1) using the equation

$$k_1 = k_2^{\frac{1}{2}}.R_{methane}/R_{ethane}^{\frac{1}{2}}\,[C_6H_5\cdot CH_3]$$

where $R_{methane}$ is the rate of formation of methane. A least-squares treatment of the results derived from the 131 runs performed with the six alkyls at about 16 mm. pressure of toluene yields the relation

$$\log k_1 = (12{\cdot}92 \pm 0{\cdot}08) - (13{,}030 \pm 270/2{\cdot}303RT)$$

if $\log k_2 = 13{\cdot}36$,[3] where the units of the bimolecular rate constants are, as throughout, $mole^{-1}$ $cm.^3$ $sec.^{-1}$, and the error limits correspond to the most probable error: systematic errors and possible errors in k_2 were disregarded. The Table lists the Arrhenius parameters for reaction (1) obtainable by a least-squares treatment of the results with each alkyl. The Arrhenius parameters obtained by use of the individual sources differ considerably from those from the complete results. The largest discrepancies are attributable to the difficulty of estimating accurately the very small quantities of ethane formed in the lower-temperature runs with the zinc and tin compounds. No rate constant falls very far from the mean line (columns 6 and 7), so it is unlikely that large systematic

[1] Price and Trotman-Dickenson, *Trans. Faraday Soc.*, 1957, **53**, (*a*) 939, (*b*) 1208; (*c*) 1958, **54**, in the press.
[2] Price, Ph.D. thesis, Edinburgh, 1958.
[3] Shepp, *J. Chem. Phys.*, 1956, **24**, 939.

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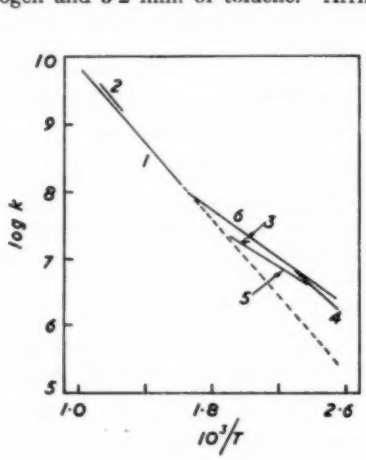
errors occur, though they are probably greater than the random errors. Unless a full mathematical analysis is made of the results, large errors can arise in the determination in a plug-flow reaction vessel of the ratios of rate constants of reactions that are of first and second order with respect to the concentration of a radical produced in a pyrolysis. In particular, the effective volume of the vessel varies with temperature, giving a low apparent activation energy for the first-order reaction. The difficulty was largely overcome by using sources with different rates of decomposition to cover the temperature range.

Radical source	Runs	log A_1	E_1	Temp.	log k_1 *	log k_1 †	Temp.
Dimethylzinc	20	13·7	16·2	573—701°	9·6	9·65	600°
Dimethylcadmium	17	11·8	12·4	469—571	9·4	9·23	500
Dimethylmercury	16	13·2	14·1	465—608	9·4	9·45	550
Trimethylantimony	30	13·3	14·3	475—582	9·4	9·41	540
Trimethylbismuth	27	13·4	12·2	346—409	8·7	8·74	390
Dimethyltin dichloride ...	21	14·6	20·2	554—637	9·6	9·69	610
Dimethylmercury [4]	15	13·0	13	518—610	9·5	9·45	550

* Rate constants for the temperature listed in last column calculated from the Arrhenius parameters for individual alkyls.

† Rate constants calculated from the least-squares line for the complete data.

Two sets of results obtained under comparable conditions have been reported. Gowenlock, Polanyi, and Warhurst [4] pyrolysed dimethylmercury in a flow system with 7 mm. of nitrogen and 3·2 mm. of toluene. Arrhenius parameters and rate constant deduced



Arrhenius plots for the abstraction of a hydrogen atom from toluene by a methyl radical.

1, This work.
2, Gowenlock, Polanyi, and Warhurst.[4]
3, Murawski, Roberts, and Szwarc.[6]
4, Szwarc and Roberts.[7]
5, Rebbert and Steacie.[8]
6, Trotman-Dickenson and Steacie.[11]

therefrom are shown in the Table. A correction of −0·2 logarithmic unit has been added to A to allow for the slightly lower value of k_2 under their conditions than in 16 mm. of toluene.[1a,5] The agreement is all that could be expected.

Only one rate constant at 230° can be deduced from the study of the pyrolysis of di-*tert.*-butyl peroxide by the toluene-carrier technique because the analyses of the products were inadequate.[6] The value of log $k_1 = 7·52$ is in reasonable agreement with ours (7·29).

Before these results can be compared with those obtained in static systems, a correction must be applied to allow for the change from a pressure of about 16 mm. to one of about 100 mm. Its exact magnitude is uncertain but must be about −0·2 logarithmic unit.[1a,5]

[4] Gowenlock, Polanyi, and Warhurst, *Proc. Roy. Soc.*, 1953, *A*, **218**, 269.
[5] Dodd and Steacie, *ibid.*, 1954, *A*, **223**, 283.
[6] Murawski, Roberts, and Szwarc, *J. Chem. Phys.*, 1951, **19**, 698.

Hence at 100 mm. $\log k_1 = 12{\cdot}7 - (13{,}000/2{\cdot}303RT)$. Szwarc and Roberts [7] obtained a similar activation energy, using the pyrolysis of di-*tert.*-butyl peroxide as a source of methyl in a static system, but their rate constants and A factors are discordant.

The apparently more reliable work of Rebbert and Steacie [8] yields $\log k_1 = 10{\cdot}6 - (7300/2{\cdot}303RT)$, which differs from our value by many times the combined experimental errors. The disagreement with the later interpretation [9] of Taylor and Smith's work,[10] $\log k_1 = 9{\cdot}8 - (7000/2{\cdot}303RT)$, is less significant as the experimental results were not very complete. The relations between all these results are shown in the Figure.

The interpretation of Trotman-Dickenson and Steacie's work on the reaction of $CD_3{\cdot}$ with toluene [11] is uncertain because it is based on a value for the rate constant of reaction (3) given [12] by $\log k_3 = 11{\cdot}4 - (10{,}300/2{\cdot}303RT)$. The experiments were done with

$$CD_3 + CD_3{\cdot}CO{\cdot}CD_3 = CD_4 + {\cdot}CD_2{\cdot}CO{\cdot}CD_3 \quad \ldots\ldots\ldots (3)$$

insufficiently deuterated acetone. More recent work indicates that [13] $\log k_3 = 11{\cdot}6 - (11{,}600/2{\cdot}303RT)$. However it is doubtful whether the results with toluene can be corrected by applying this value for k_3 which would give $\log k_1 = 11{\cdot}2 - (9600/2{\cdot}303RT)$. The true value probably lies somewhere between this expression and that originally proposed: $\log k_1 = 11{\cdot}0 - (8300/2{\cdot}303RT)$. It can be maintained that results from both low-temperature photolyses and high-temperature flow experiments are correct within the limits of the experimental errors and that the Arrhenius plot is really curved owing to a change in mechanism with temperature. Perhaps the strongest argument against this conclusion is the very high A factor which the high-temperature reaction would require. Some fifty metatheses of methyl radicals have been studied; [14] as predicted by transition-state theory, none has a well-established A factor greater than $10^{12{\cdot}0}$. Further investigation of this reaction, particularly in the range 250—450°, is needed.

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[7] Szwarc and Roberts, *Trans. Faraday Soc.*, 1950, **46**, 625.
[8] Rebbert and Steacie, *J. Chem. Phys.*, 1953, **21**, 1723.
[9] Trotman-Dickenson and Steacie, *J. Phys. Chem.*, 1951, **55**, 908.
[10] Taylor and Smith, *J. Chem. Phys.*, 1940, **8**, 543.
[11] Trotman-Dickenson and Steacie, *ibid.*, 1951, **19**, 329.
[12] *Idem*, *ibid.*, 1950, **18**, 1097.
[13] Whittle and Steacie, *ibid.*, 1953, **21**, 993; McNesby, Davis, and Gordon, *J. Amer. Chem. Soc.*, 1954, **76**, 823.
[14] Trotman-Dickenson, "Gas Kinetics," Butterworths, London, 1955.

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852. *Complex Formation involving Silver and the 2-Hydroxyethylamines.*

By D. J. ALNER and A. G. SMEETH.

STABILITIES of complexes between silver salts and 2-hydroxyethylamines were previously determined by pH methods.[1] We have measured the solubility of silver oxide in solutions of mono-, bis-, and tris-2-hydroxyethylamines ("ethanolamines"); together with data obtained electrometrically it again demonstrates formation of complexes, whose compositions and stability constants are correlated with the basic strengths of the amines.

Experimental.—Dissociation constants of the 2-hydroxyethylamines at 20°. Distilled under reduced pressure, the purified amines (99·7% w/w in each case, by titration with hydrochloric

[1] Bjerrum, "Metal Ammine Formation in Aqueous Solution," Haase, Copenhagen, 1941.

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acid) were characterised through refractive indices (Hilger–Chance refractometer): 2-Hydroxyethylamine, n_D^{20} 1·4545 (lit.,[2,3] 1·4539; lit.,[4] for sample containing 97%, n_D^{20} 1·4544); bis-2-hydroxyethylamine, n_D^{20} 1·4780 (lit.,[2] 1·4776); tris-2-hydroxyethylamine, n_D^{20} 1·4851 (lit.,[2] 1·4851). Dissociation constants of the amines were determined by measuring the hydrogen-ion activities set up during the neutralisation in the cell:

$$H_2(1 \text{ atm.}) \mid \text{Base} + \text{HCl} \mid \text{KCl bridge} \mid \text{Sat. calomel}$$

Dilute solutions of the bases were titrated with hydrochloric acid at 20°, and the pH values, as defined by $-\log\{H^+\}$, where braces {} represent activities, were calculated from the measured e.m.f's. These titrations are represented in Table 1; K refers to the equilibrium $B + H_2O \rightleftharpoons BH^+ + OH^-$; $K = \{BH^+\}\{OH^-\}/\{B\}$; I is the ionic strength.

TABLE 1. *Dissociation constants at* 20°

2-Hydroxyethylamine

HCl (ml.)	pH (obs.)	10^3I	pK		HCl (ml.)	pH (obs.)	10^3I	pK	
50 *ml.* of 0·0494M-*base titrated with* 0·50M-HCl					50 *ml.* of 0·00988M-*base titrated with* 0·100M-HCl				
1·00	10·22	0·98	4·59		1·00	10·15	1·96	4·61	
1·50	10·00	1·46	4·58		1·50	9·94	2·91	4·59	
2·00	9·82	1·92	4·58		2·00	9·77	3·85	4·59	
2·50	9·64	2·38	4·59		2·50	9·59	4·76	4·59	
3·00	9·47	2·83	4·58		3·00	9·41	5·66	4·58	
3·50	9·27	3·27	4·59		3·50	9·19	6·54	4·60	Mean 4·59
4·00	9·02	3·70	4·60	Mean 4·59					

Bis-2-hydroxyethylamine

50 *ml. of* 0·0505M-*base titrated with* 0·50M-HCl					50 *ml. of* 0·10M-*base titrated with* 0·100M-HCl				
1·00	9·64	0·98	5·22		1·00	9·59	1·96	5·20	
1·50	9·41	1·46	5·19		1·50	9·37	2·91	5·20	
2·00	9·22	1·92	5·19		2·00	9·19	3·85	5·19	
2·50	9·06	2·38	5·19		2·50	9·01	4·76	5·20	
3·00	8·88	2·83	5·20		3·00	8·84	5·66	5·20	
3·50	8·70	3·27	5·19		3·50	8·64	6·54	5·21	Mean 5·20
4·00	8·47	3·70	5·20	Mean 5·20					

Tris-2-hydroxyethylamine

50 *ml.* of 0·050M-*base titrated with* 0·50M-HCl					50 ml. *of* 0·01M-*base titrated with* 0·100M-HCl				
1·00	8·84	0·98	6·34		1·00	8·46	1·96	6·33	
1·50	8·25	1·46	6·34		1·50	8·22	2·91	6·34	
2·00	8·06	1·92	6·35		2·00	8·04	3·85	6·33	
2·50	7·89	2·38	6·35		2·50	7·86	4·76	6·34	
3·00	7·71	2·83	6·36		3·00	7·68	5·66	6·35	
3·50	7·52	3·27	6·36		3·50	7·49	6·54	6·35	
4·00	7·29	3·70	6·36	Mean 6·35	4·00	7·25	7·41	6·36	Mean 6·35

Corrections were applied for the extent of ionisation of the uncombined base, and for the hydrolysis of the amine hydrochloride formed. The activity coefficients of the univalent ions were calculated from $-\log f = 0{\cdot}505\sqrt{I}/(1 + \sqrt{I})$,[5] the activity coefficient of the un-ionised, uncombined base being assumed to be unity.

Dissociation constants of the 2-hydroxyethylamines at 20° are new. Our values represent true activity constants, and although close to those found [6] for solutions of greater ionic strength at 25°, differ from them by an activity factor.

Solubility product K_s of silver oxide at 20°. Variations in pH were measured with a glass

[2] Knorr, *Ber.*, 1897, **30**, 909.
[3] Reitmeier, Sivertz, and Tartar, *J. Amer. Chem. Soc.*, 1940, **62**, 1943.
[4] Leibush and Shorina, *J. Appl. Chem., U.S.S.R.*, 1947, **20**, 691.
[5] Guggenheim and Schindler, *J. Phys. Chem.*, 1934, **38**, 539.
[6] *E.g.*, Bruehlman and Verhoek, *J. Amer. Chem. Soc.*, 1948, **70**, 1401; Bjerrum, *Chem. Rev.*, 1950, **46**, 381; Bjerrum and Refn, *Suomen Kem.*, 1956, *B*, **29**, 68.

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electrode (with exclusion of carbon dioxide) during titrations of dilute solutions of silver nitrate with carbonate-free sodium hydroxide (Table 2).

It was assumed that silver hydroxide was precipitated stoicheiometrically, since no basic salt appeared to be formed; the inflexion in the pH curve appeared at the stoicheiometric end-point. From the concentrations and ionic strengths used, the activities of the silver ions remaining in solution were calculated, the negligible solubility of the precipitate being ignored.

We used our value, a true constant for $K_s = \{Ag^+\}\{OH^-\} = 1{\cdot}413 \times 10^{-8}$ at 20°, which agrees well with concentration solubility products $[Ag^+][OH^-]$ [$1{\cdot}44 \times 10^{-8}$ (ref. 7); $3{\cdot}42 \times 10^{-8}$ (ref. 8)], in deriving the stability constants for the complexes.

TABLE 2. *Titration of* 0·01M-*silver nitrate* (100 *ml.*) *with* 0·10M-*sodium hydroxide at* 20°.

NaOH (ml.)	1·00	2·00	3·00	4·00	5·00	6·00	7·00	8·00
pH (obs.)	8·36	8·46	8·53	8·61	8·69	8·79	8·92	9·10
10^2I	0·990	0·980	0·979	0·962	0·952	0·943	0·933	0·926
pK_s	7·90	7·86	7·85	7·86	7·85	7·85	7·85	7·85

Solubility of silver oxide in aqueous solutions of the 2-hydroxyethylamines at 20°. Tamisier [9] determined the solubility of silver chloride (but not the oxide) in solutions of 2-hydroxyethylamine and demonstrated complex formation.

Silver hydroxide was precipitated from dilute silver nitrate solution with the stoicheiometric amount of sodium hydroxide, washed with hot water until free from electrolytes, and filtered. Excess of the moist silver oxide was added to solutions of the amines of known concentration, and shaken mechanically in black bottles at 20° until equilibrium was reached.

TABLE 3. *Solubility of silver oxide at* 20°.

2-Hydroxyethylamine				Bis-2-hydroxyethylamine				Tris-2-hydroxyethylamine			
Base (10^{-2}N)	Ag_2O (10^{-3}N)	pH (obs.)	log β_2	Base (10^{-2}N)	Ag_2O (10^{-3}N)	pH (obs.)	log β_2	Base (10^{-2}N)	Ag_2O (10^{-3}N)	pH (obs.)	log β_2
5·1	1·1	11·98	6·91	5·0	4·2	11·72	5·80	10·1	1·6	11·35	4·24
10·2	2·25	12·31	6·91	10·0	8·6	11·98	5·80	15·2	2·4	11·53	4·23
15·3	3·45	12·48	6·92	15·0	13·2	12·12	5·81	20·2	3·2	11·64	4·22
20·4	4·67	12·55	6·92	20·0	17·8	12·23	5·80	25·3	4·0	11·73	4·22
22·5	5·86	12·61	6·91	25·0	22·4	12·31	5·81				Mean 4·23
		Mean	6·91			Mean	5·80				

The pH's of these solutions were determined with a glass electrode, and the silver content of the clear filtrates by Volhard's thiocyanate method. Table 3 gives our results, together with calculated values of the stability constants of the silver complexes, as defined by $\beta_2 = \{AgB_2^+\}/\{Ag^+\}\{B\}^2$.

Discussion.—The high pH values found in the amine solutions saturated with silver oxide (Table 3) demonstrated that strong bases of the type AgB_2OH were formed, since the bases themselves could not cause them. The solubility can be explained in terms of the stability constant of the complex cation formed and of the solubility product of silver hydroxide, or conversely can be used to calculate the stability constant of the complex cation.

The combination of silver hydroxide with the base can be represented by $AgOH + nB \rightleftharpoons AgB_n^+ + OH^-$. The complex cation itself must be in equilibrium with silver ions, $AgB_n^+ \rightleftharpoons Ag^+ + nB$, hence $\beta_n = \{AgB_n^+\}/\{Ag^+\}\{B\}^n$.

If the concentration of base is C equiv./l., the amount of silver hydroxide dissolved

[7] Laue, *Z. anorg. Chem.*, 1927, **165**, 324.
[8] Noyes and Kohr, *J. Amer. Chem. Soc.*, 1902, **24**, 144; Whitby, *Z. anorg. Chem.*, 1910, **67**, 387.
[9] Tamisier, *Bull. Soc. chim. France*, 1933, **53**, 156.

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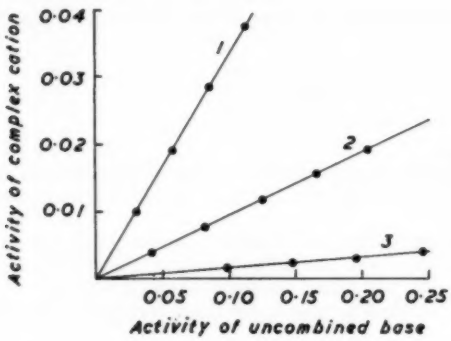
S equiv./l., and f is the activity coefficient (calc.) of the univalent ions, then $Sf = \{AgB_n^+\} = \{OH^-\}$. The excesses of the amines can be considered as being un-ionised because of the ionisation of the complex base; thus, the activity coefficient being assumed to be unity, then $(C - nS)$ equiv./l. is the concentration, and hence the activity of the un-ionised, uncombined amine B. Since the solution was also saturated with silver oxide, $\{Ag^+\}\{OH^-\} = K_s$, whence $\beta_n = (fS)^2/K_s(C - nS)^n$. If n has the most probable value of 2 in the case of silver, then $fS = K'(C - 2S)$, where $K' = \sqrt{(\beta_n K_s)}$, and a plot of the activity of the complex cation against the activity of the excess of uncombined base should be straight (see Figure).



1, 2-Hydroxyethylamine.
2, Bis-2-hydroxyethylamine.
3, Tris-2-hydroxyethylamine.

The dissociation constants show the order of basic strengths to be mono- > bis- > tris-2-hydroxyethylamine. The stabilities of the complex cations formed between silver and these bases are in the same order.

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853. *Reactions with Asymmetric Diarylethylenes. Part V.*[1] *Conversion of* 2 : 2-*Di*-p-*alkoxyphenylvinyl Chloride or Bromide in Alkaline Medium into the Corresponding Tolane.*

By WADIE TADROS, ALFY BADIE SAKLA, and MOHEB SADEK ISHAK.

THE mechanism of conversion of 2 : 2-di-*p*-alkoxyphenylvinyl chlorides or bromides into 1 : 1 : 4 : 4-tetra-arylbuta-1 : 3-dienes has been already discussed.[1] On the other hand, they are converted by alcoholic sodium ethoxide at 180—200° in a sealed tube [2,3] (however, neither the quantity nor the concentration of the reagent was specified) or by potassium amide in liquid ammonia [4,5] into the corresponding tolanes. The mechanism of the reaction has been discussed by Coleman, Holst, and Maxwell,[5] but comment on this is postponed. However, Harris and Frankforter's statement [3] that 2 : 2-di-*p*-methoxy(or

[1] Part IV, Tadros and Sakla, *J.*, 1957, 3210.
[2] Wiechell, *Annalen*, 1894, **279**, 337.
[3] Harris and Frankforter, *J. Amer. Chem. Soc.*, 1926, **48**, 3144.
[4] Coleman and Maxwell, *ibid.*, 1934, **56**, 132.
[5] Coleman, Holst, and Maxwell, *ibid.*, 1936, **58**, 2310.

ethoxy)phenylvinyl bromide gave rise to the tolane when treated with ethanolic sodium ethoxide on the water-bath, could not be substantiated by us.

The present paper reports a preliminary study of this reaction effected with sodium 2-hydroxyethoxide in ethylene glycol. The vinyl bromide reacted more readily than the chloride. As pointed out by Coleman and Maxwell,[4] it is notable that in these arrangements a given substituent in the *para*-position in the phenyl group is found in the *para*-position in the tolane. A mixture of 2 : 2-di-*p*-methoxy- and 2 : 2-di-*p*-ethoxy-phenylvinyl bromide gave both 4 : 4'-dimethoxy- and 4 : 4'-diethoxy-tolane, but no mixed tolane. Pending confirmation we assume that the reaction is intramolecular, but the formation of the 4 : 4'-disubstituted tolanes indicates that, although the migrating aryl group suffers complete severance, it may have remained in the domain of the molecule. 4-Ethoxy-4'-methoxytolane was obtained from both forms of 2-*p*-ethoxyphenyl-2-*p*-methoxyphenylvinyl bromide obtained by bromination of 1-*p*-ethoxyphenyl-1-*p*-methoxyphenylethylene. Partial demethylation usually accompanied formation of the tolanes, in amounts dependent on the time of the reaction. When the alkaline filtrate, after the removal of 4 : 4'-dimethoxytolane, was acidified *p*-hydroxyphenyl 4'-methoxybenzyl ketone was obtained;[6] this is also obtained when the 4 : 4'-dimethoxytolane is similarly treated. With 2-*p*-ethoxyphenyl-2-*p*-methoxyphenylvinyl bromide, acidification of the alkaline filtrate gave 4-ethoxybenzyl *p*-hydroxyphenyl ketone, the structure of which was proved by comparison of the methylation products of the two possible isomers.[7]

Experimental.—*4-Ethoxy-4'-methoxybenzophenone.* Prepared by Friedel–Crafts[8] reaction or by ethylation of 4-hydroxy-4'-methoxybenzophenone[9] (2·28 g. of ketone, 0·37 g. of sodium dissolved in 50 c.c. of alcohol; 2·34 g. of ethyl iodide), this ketone, crystallised from alcohol, had m. p. 112° (Found: C, 74·8; H, 6·0. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·25%).

1-p-*Ethoxyphenyl*-1-p-*methoxyphenylethylene* was prepared by Grignard reactions. (*a*) 4-Ethoxy-4'-methoxybenzophenone (25·6 g.) was added to the Grignard reagent (magnesium, 3·6 g.; methyl iodide, 21·3 g.; ether, 200 c.c.). Decomposition with aqueous ammonium chloride and extraction with ether gave the ethylene (21 g.) which, separated from alcohol, had m. p. 124° (Found: C, 80·0; H, 7·0. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·3%). (*b*) 4-Ethoxyacetophenone (16·4 g.) was added to the Grignard reagent (magnesium, 3·6 g.; *p*-bromoanisole, 28 g.; ether, 200 c.c.) and afforded 19 g. of the ethylene.

2-p-*Ethoxyphenyl*-2-p-*methoxyphenylvinyl bromides.* The product from bromine (8·0 g.) and the ethylene (12·7 g.) in ether (270 c.c.) was washed with 10% aqueous sodium hydroxide, followed by water, and after recovery was heated on the water-bath with sodium hydroxide (3 g.) in alcohol (60 c.c.) for 30 min., diluted with water, cooled, filtered, and washed with water. Recrystallisation from alcohol or light petroleum (b. p. 50—70°) gave two fractions of bromide: (i) m. p. 70—72°; (ii) m. p. 48—50° (Found: Br, 23·6. Calc. for $C_{17}H_{17}O_2Br$: Br, 24·0%).

Action of sodium 2-hydroxyethoxide in ethylene glycol on 2 : 2-*di*-p-*alkoxyphenylvinyl halide.* (*a*) The procedure and products obtained are exemplified as follows: 2 : 2-Di-*p*-methoxyphenylvinyl bromide (1·595 g.) and a solution from sodium (0·23 g.) in ethylene glycol (15 c.c.) were boiled for 5 hr., then cooled and diluted with water, and the precipitate was filtered off. 4 : 4'-Dimethoxytolane separated from alcohol or acetic acid as colourless crystals (0·8 g.), m. p. 142—143° (Found: C, 80·3; H, 5·9. Calc. for $C_{16}H_{14}O_2$: C, 80·7; H, 5·9%). Acidification of the alkaline filtrate with acetic or hydrochloric acid and recrystallisation of the precipitate from dilute alcohol gave *p*-hydroxyphenyl 4'-methoxybenzyl ketone (0·4 g.; m. p. and mixed m. p. 175°). Ethylation gave *p*-ethoxyphenyl 4'-methoxybenzyl ketone, m. p. and mixed m. p. 101—102°. Other tolanes were similarly obtained (yield *ca.* 90—95%) and recrystallised from alcohol or acetic acid as colourless crystals: 4 : 4'-diethoxy-, m. p. 162—163° (Found: C, 81·1; H, 6·7. Calc. for $C_{18}H_{18}O_2$: C, 81·2; H, 6·8%); 4 : 4'-*di*-n-*propoxy*-, m. p. 133—135° (Found:

[6] Tadros, Ekladius, and Sakla, *J.*, 1954, 2351.
[7] Carter and Hey, *J.*, 1948, 150.
[8] Schönberg, Schütz, and Nickel, *Ber.*, 1928, **61**, 1375; Migita, *Bull. Chem. Soc. Japan*, 1932, **7**, 341; Jones, *J.*, 1936, 1854.
[9] Auwers, *Ber.*, 1903, **36**, 3893.

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C, 81·2; H, 7·4. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%); 4 : 4′-*diisopropoxy-*, m. p. 162—165° (Found: C, 81·3; H, 7·1. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%); 4 : 4′-*di*-n-*butoxy-tolane*, m. p. 127—128° (Found: C, 81·6; H, 8·0. $C_{28}H_{30}O_2$ requires C, 82·0; H, 8·45%).

(ii) The tolane (0·1 g.) was obtained when the above experiment was repeated with the di-*p*-ethoxyvinyl chloride (1·51 g.). Using 0·575 g. of sodium gave 0·5 g. of tolane.

(iii) 2-*p*-Ethoxyphenyl-2-*p*-methoxyphenylvinyl bromide, m. p. 48—50° or 70—72° (1·665 g.), and sodium (0·23 g.) in ethylene glycol (15 c.c.) were treated as above. *4-Ethoxy-4′-methoxytolane* (0·8 g.), crystallised from acetic acid, had m. p. 138—139° (Found: C, 80·6; H, 6·3. $C_{17}H_{16}O_2$ requires C, 81·0; H, 6·3%). Acidification of the alkaline filtrate yielded *4-ethoxybenzyl 4′-hydroxyphenyl ketone* (0·3 g.), m. p. 160—162° (from dilute alcohol) (Found: C, 74·6; H, 6·2. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·25%). With dimethyl sulphate it gave 4-ethoxybenzyl *p*-methoxyphenyl ketone, m. p. and mixed m. p. 100°.

*Reaction with 2 : 2-di-*p*-methoxy- and 2 : 2-di-*p*-ethoxy-phenylvinyl bromides.* Repeating experiment (i) with equimolecular quantities of 2 : 2-di-*p*-methoxy- (1·595 g.) and 2 : 2-di-*p*-ethoxy-phenylvinyl bromide (1·735 g.), sodium (0·46 g.), and ethylene glycol (30 c.c.) gave 4 : 4′-diethoxytolane (1·1 g.), m. p. 162—163°, separating readily at room temperature from acetic acid. Dilution of the acetic acid mother-liquor and recrystallisation from alcohol gave 4 : 4′-dimethoxytolane (0·5 g.), m. p. and mixed m. p. 142—143°. On acidification of the alkaline mother-liquor gave *p*-hydroxyphenyl 4′-methoxybenzyl ketone (0·3 g.), m. p. and mixed m. p. 175°. It is remarkable that dealkylation occurs more readily with the methoxyl group.

Action of sodium 2-hydroxyethoxide in ethylene glycol on 4 : 4′-dimethoxytolane. 4 : 4′-Dimethoxytolane (1·195 g.) and sodium (0·23 g.) in ethylene glycol (15 c.c.) were heated at the b. p. for 5 hr. Dilution with water gave unchanged tolane (0·5 g.). Acidification of the alkaline filtrate gave 4-hydroxyphenyl 4′-methoxybenzyl ketone (0·3 g.).

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854. o-*Cyanophenylhydrazine and* 3-*Aminoindazole.*

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THE reduction of 3 : 4-dihydro-4-hydroxyimino-1 : 2 : 3-benzotriazine by stannous chloride and hydrochloric acid gave a compound to which Pinnow and Sämann [1] assigned the constitution 1 : 2-(or 2 : 3-)dihydro-1 : 2 : 3-benzotriazine. Gabriel [2] thought this compound to be identical with one he obtained by reducing diazotised *o*-cyanoaniline with stannous chloride and which he considered to be *o*-cyanophenylhydrazine. Reissert and Grube record,[3] however, that a similar reduction gave, instead of *o*-cyanophenylhydrazine, the isomeric 3-aminoindazole; Kwartler and Lucas [4] used a similar route to 3-aminoindazole. The close similarity of the recorded properties of Gabriel's compound to those of 3-aminoindazole [5] prompted direct comparison.

3-Aminoindazole can be obtained by coupling *o*-tolyldiazonium chloride with indazole and reducing the resulting azo-compound with ammonium sulphide [5] or sodium dithionite: this, together with its possession of an amino-group capable of being diazotised and hence conversion into the known 3-chloroindazole,[5] is adequate proof of structure. Samples of compounds prepared by the methods of Pinnow and Sämann,[1] of Gabriel,[2] and of

[1] Pinnow and Sämann, *Ber.*, 1896, **29**, 623.
[2] Gabriel, *Ber.*, 1903, **36**, 800.
[3] Reissert and Grube, *Ber.*, 1909, **42**, 3710.
[4] Kwartler and Lucas, *J. Amer. Chem. Soc.*, 1943, **65**, 1804.
[5] Bamberger and von Goldberger, *Annalen*, 1899, **305**, 339.

Reissert and Grube [3] have been compared with an authentic specimen of 3-aminoindazole (m. p. and mixed m. p. of bases, picrates, diacetyl and dibenzoyl derivatives; ultraviolet absorption spectra); the results show the so-called *o*-cyanophenylhydrazine to be identical with 3-aminoindazole.

Experimental.—3-Aminoindazole. (*a*) To a solution of 3-*o*-tolylazoindazole [5] (3·55 g.) in ethanol (50 ml.) were added sodium hydroxide (2·5 g.) and sodium dithionite (6·2 g.) in water (50 ml.). The mixture was refluxed for 30 min., evaporated to about 30 ml. at 60°/15 mm., and then steam-distilled to remove *o*-toluidine (benzoyl derivative, m. p. and mixed m. p. 144—145°). Extraction of the cooled residue with ether gave 3-aminoindazole (2·00 g.; 100%), which crystallised from benzene as plates, m. p. 154·5—155° (Found: C, 63·1; H, 5·15. Calc. for $C_7H_7N_3$: C, 63·15; H, 5·3%). Its *picrate*, needles from glacial acetic acid, had m. p. 236° (decomp.) (Found: C, 43·3; H, 2·75; N, 23·1. $C_{13}H_{10}O_7N_6$ requires C, 43·1; H, 2·8; N, 23·2%). The diacetyl derivative, needles from benzene, had m. p. 181—181·5° (Found: C, 61·2; H, 4·95; N, 19·05. Calc. for $C_{11}H_{11}O_2N_3$: C, 60·8; H, 5·1; N, 19·35%): the dibenzoyl derivative, needles from ethanol, had m. p. 183—184° (Found: C, 73·8; H, 4·35. Calc. for $C_{21}H_{15}O_2N_3$: C, 73·85; H, 4·45%). Bamberger and von Goldberger record m. p. 153·5—154·5°, 177—178°, and 182° for the base, its diacetyl, and its dibenzoyl derivative, respectively.[5]

(*b*) A well-stirred ice-cold solution of diazotised sulphanilic acid (4·5 g.) and indazole (3·0 g.) in dilute hydrochloric acid was slowly made alkaline with sodium hydroxide solution. Next day, after precipitated indazole (2·01 g.) had been removed, reduction of the filtrate with sodium dithionite afforded 3-aminoindazole (0·20 g.), m. p. and mixed m. p. 154·5—155°.

Below are recorded m. p.s of bases and derivatives made by the methods of Pinnow and Sämann [1] (A), Gabriel [2] (B), and Reissert and Grube [3] (C): there was no depression of m. p. on admixture, as appropriate, with 3-aminoindazole or its derivatives.

	M, p.s			
	Base	Picrate	Diacetyl derivative	Dibenzoyl derivative
A	155—155·5°	237—238° (decomp.)	180·5—181·5°	184·5—185·5°
B	154·5—155	236—237 (decomp.)	181—182	184·5—185
C	154—155	236—237 (decomp.)	181—182	183·5—184·5

The ultraviolet absorption spectra of the bases were determined in ethanol ($\lambda_{max.}$ in mμ; ε in parentheses). Figures in italics denote submerged maxima.

	Absorption maxima		
A	217(21,800)	*ca. 260*(1380)	310(4410)
B	217(20,100)	*ca. 260*(1330)	310(4300)
C	217(22,200)	*ca. 260*(1290)	310(4370)
3-Aminoindazole	217(20,500)	*ca. 260*(1300)	310(4500)

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XUM

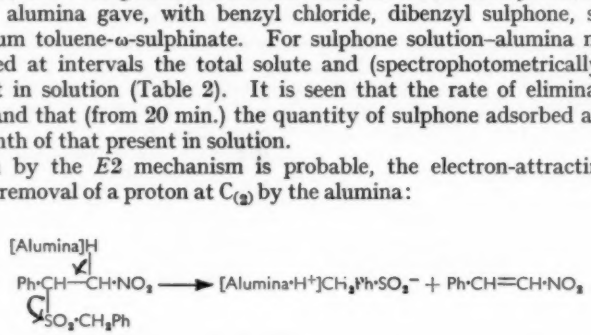
855. *The Decomposition of 2-Nitro-1-phenylethyl Sulphones at an Alumina Surface.*

By C. L. Arcus and P. A. Hallgarten.

During attempts to separate optically active α-methylphenethyl 2-nitro-1-phenylethyl sulphones from other compounds by chromatography on alumina, losses in rotatory power were noticed, and it was further found that acetone solutions of the (+)-sulphone-A (assigned [1] the l_Rd_α configuration, where the suffix R refers to the α-methylphenethyl and α to the 2-nitro-1-phenylethyl group), on treatment with alumina, undergo progressive racemisation. β-Nitrostyrene was isolated from the solutions, so that elimination had occurred, accounting for part of the loss in rotatory power. The recovered sulphone had a lowered m. p., so that racemisation at one or both centres had contributed to the fall in rotation, but it was not practicable to determine the proportion of the four diastereoisomers in the recovered material.

For further investigation, (±)-benzyl 2-nitro-1-phenylethyl sulphone was used; its acetone solution, after being shaken with alumina, yielded β-nitrostyrene, and an alkaline extract of the alumina gave, with benzyl chloride, dibenzyl sulphone, so that it had contained sodium toluene-ω-sulphinate. For sulphone solution–alumina mixtures, there were determined at intervals the total solute and (spectrophotometrically) the β-nitrostyrene present in solution (Table 2). It is seen that the rate of elimination decreases progressively, and that (from 20 min.) the quantity of sulphone adsorbed at any one time is about one-tenth of that present in solution.

Elimination by the *E*2 mechanism is probable, the electron-attracting nitro-group facilitating the removal of a proton at $C_{(2)}$ by the alumina:



The results illustrate the unsuitability, which has been noted in other connections,[2] of chromatography on alumina for the separation of compounds susceptible to proton-removal.

Experimental.—M. p.s are corrected.

Alumina (100 g.) was heated on a steam-bath for 2 hr. with acetic acid (150 ml.) and methanol (15 ml.), kept overnight, and reheated for 5 hr. The acid was decanted and the alumina washed with cold, then hot, methanol, and dried, first at 80°, then at 160°. Acetone was refluxed for 8 hr. with potassium permanganate, then distilled, and redistilled from potassium carbonate. Treatment of solutions with alumina was carried out at 25·5° ± 0·5°.

Table 1.

Time, min.	0	13	61	130	285	1470	2730
α^{25}_{5893}	1·12°	0·92°	0·70°	0·73°	0·60°	0·42°	0·11°

A solution of (+)-α-methylphenethyl 2-nitro-1-phenylethyl sulphone-A (m. p. 140·5°; 0·201 g.) in acetone (8·0 ml.) was shaken intermittently with alumina (1·002 g.). The rotatory power (*l*, 1·0) fell (Table 1). Sublimation (60°/1 mm.) of the product from evaporation of the

[1] Arcus and Hallgarten, *J.*, 1957, 3407.

[2] E. and M. Lederer, "Chromatography," Elsevier Publ. Co., Amsterdam, 2nd edn., 1957, pp. 61—65.

solution gave β-nitrostyrene (19 mg.), m. p. 56°, mixed m. p. 56·5°. The remaining sulphone (0·11 g.) had m. p. 124—125° and, after recrystallisation, m. p. 137·5° and m. p. 140° when mixed with the original sulphone. (The sulphones-A are the less-soluble diastereoisomers.[1])

Toluene-ω-thiol (22·0 g.) and β-nitrostyrene (26·5 g.) were heated under coal-gas for 9 hr. at 120° with benzoyl peroxide (0·1 g.). The product solidified after a week, and, on being washed with ice-cold methanol, yielded benzyl 2-nitro-1-phenylethyl sulphide, m. p. 39° (Found: N, 5·0; S, 11·3. Calc. for $C_{15}H_{15}O_2NS$: N, 5·1; S, 11·7%). To the sulphide (22·0 g.) in acetic acid (50 ml.) was added acetic acid–34% hydrogen peroxide (25 ml. each), the whole being kept below 40°. Next day the product was collected, washed with acetic acid and with methanol, and recrystallised from acetone–methanol, yielding benzyl 2-nitro-1-phenylethyl sulphone (10·5 g., 43%), m. p. 140—140·5°. Cason and Wanser [3] obtained the sulphide as an oil which on oxidation at 100° gave the sulphone in 18% yield.

(*a*) Benzyl 2-nitro-1-phenylethyl sulphone (1·0 g.) in acetone (27 ml.), intermittently shaken for 8 hr. with alumina (5·0 g.), gave β-nitrostyrene (0·15 g.), m. p. and mixed m. p. 56·5—57°, and unchanged sulphone (0·56 g.), m. p. 139—140°, mixed m. p. 140·5°.

(*b*) The sulphone (10·5 g.) in acetone (125 ml.) was mechanically shaken for several days with alumina (32 g.). The latter was separated and washed with acetone, then shaken with 0·2N-sodium hydroxide (20 ml.); the extract was filtered, then boiled with benzyl chloride (1 g.) for 1 hr. After removal of excess of benzyl chloride by passage of steam, the whole was extracted with chloroform. The product from the extract was washed with methanol and recrystallised from ethanol; it yielded dibenzyl sulphone, m. p. 150° (Found: O, 13·5; S, 13·4. Calc. for $C_{14}H_{14}O_2S$: O, 13·0; S, 13·0%). Fromm and de Seixas Palma [4] record m. p. 151°.

(*c*) In each experiment of Table 2, benzyl 2-nitro-1-phenylethyl sulphone (0·500 g.) in acetone (12·5 ml.) was shaken at constant speed with alumina (2·50 g.). After the stated time the solution was filtered through sintered glass, and the concentration of β-nitrostyrene determined by use, at 420 mμ, of a Unicam S.P. 600 spectrophotometer. By evaporation of the filtrate the total solute was determined, and hence, by difference, the sulphone in solution. β-Nitrostyrene was not detectably adsorbed by alumina during 24 hr. under the conditions used.

TABLE 2. *Decomposition of benzyl 2-nitro-1-phenylethyl sulphone on alumina.*

Time (min.)	11	20	30	45	60	65	95	120	152	180	208	6 days
β-Nitrostyrene, (*a*) *	4	7	8	9	10	13	13	14	14	16	15	20
Sulphone in soln., (*b*) *	68	85	79	84	82	79	76	82	81	75	75	70
100 − (*a* + *b*)	28	8	13	7	8	8	11	4	5	9	10	10

* As moles % of the original sulphone.

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[3] Cason and Wanser, *J. Amer. Chem. Soc.*, 1951, **73**, 142.
[4] Fromm and de Seixas Palma, *Ber.*, 1906, **39**, 3319.

XUM

856. *The Isolation of Solasodine from the Berries of* Solanum macranthum.

By D. A. H. Taylor.

Solanum macranthum is a large shrub or small tree, commonly planted in the tropics. It has blue flowers, and berries similar in size to tomatoes. Hydrolysis of the juice of the minced green berries gave an insoluble hydrochloride, from which only solasodine was obtained on basification. Extraction of the basified mother liquor gave, after chromatography, solaso-3 : 5-diene. The author is grateful to Dr. R. K. Callow for infrared spectra, and to Mr. G. K. Berrie, of the College Department of Botany, for identification of the specimen, growing on the College site.

Experimental.—*Solanum macranthum* berries (3·94 kg.) were minced and the juice (2·75 l.) expressed through cloth. This was mixed with methanol (2·75 l.) and kept for three days. After centrifugation, concentrated hydrochloric acid (275 c.c.) was added, the solution refluxed for 1 hr., and concentrated to 2 l. under reduced pressure. The precipitated hydrochloride was filtered, shaken with chloroform and concentrated aqueous ammonia, and the chloroform layer evaporated. The crystalline residue was taken up in benzene and chromatographed on alumina (50 g.). Benzene containing chloroform (25%) eluted solasodine, which recrystallised from acetone–chloroform as colourless crystals (3·7 g.), m. p. 201°, $[\alpha]_D^{20}$ (MeOH) −100° (Found: C, 74·7; H, 10·5; O, 11·3; N, 3·3. Calc. for $C_{27}H_{43}O_2N,H_2O$: C, 75·1; H, 10·5; O, 11·1; N, 3·25%). The infrared spectrum was identical with an authentic sample kindly provided by Professor L. H. Briggs. The basified mother liquor was extracted with chloroform and the extract chromatographed on alumina. Light petroleum (b. p. 60—80°) containing chloroform eluted a solid which crystallised from acetone–chloroform as shining plates of solaso-3 : 5-diene (130 mg.), m. p. 170°, $[\alpha]_D^{20}$ ($CHCl_3$) −180°, $\lambda_{max.}$ (hexane) 236 mμ (log ε 4·3) (Found: C, 81·4; H, 10·4; O, 4·6. Calc. for $C_{27}H_{41}ON$: C, 82·0; H, 10·45; O, 4·0%). The physical properties agree with those recorded in the literature.[1]

University College, Ibadan, Nigeria. [*Received, July 24th*, 1958.]

[1] Prelog and Jeger, "The Alkaloids," vol. iii, ed. Holmes and Manske, Academic Press Inc., New York, 1953, p. 265.

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